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TREATMENT OF MYASTHENIA GRAVIS

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Myasthenia gravis is a rare disease. Viets [1] has estimated that the total number of cases in the United States is about 1,500. In spite of this, there is widespread interest in the disease because of the challenge presented with regard to its cause and treatment, because of the complex nature of the pathologic physiology involved and because modern advances in biologic chemistry have afforded a new array of technics for its study. Consequently, there is considerable literature dealing with the condition from groups of investigators with widely differing interests and approaches.

CLINICAL FEATURES

The classic clinical picture of myasthenia gravis permits its easy recognition. The undue fatigue of voluntary muscles after exercise, their return to normal or near normal after rest, the absence of muscular atrophy, the mildness of symptoms in the forenoon as compared with the afternoon and evening, the variable clinical course which may be interspersed with spontaneous remissions and relapses and the failure on neurologic examination to demonstrate evidence of structural changes either in the central nervous system or peripheral nerves have enabled physicians accurately to diagnose the disease long before the advent of specific measures for its detection.

The muscles most frequently affected are those concerned with extraocular movements, the involvement of which results in ptosis, strabismus and diplopia in approximately 60 per cent of cases. Then in order of frequency occur generalized weakness, weakness of the extremities, dysarthria, dysphagia, difficulty in mastication, weakness of the facial muscles and weakness of the muscles of the neck. There may be many variable combinations of muscle group weakness which may show shifting from one set of muscles to another as the disease progresses. Untreated, the disease runs a fatal course in 50 to 75 per cent of cases in a few years, but under present methods of therapy the mortality rate is probably about 10 per cent.[1] Death usually results from respiratory paralysis or bronchopneumonia of the aspiration type.

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1. Viets, H. R.: Diagnosis and Treatment of Myasthenia Gravis, Postgrad. Med. **4**: 55 (July) 1948.

DIAGNOSIS

To make the diagnosis certain, several highly specific procedures are available. The most satisfactory of these is the intramuscular administration of 1.5 mg. neostigmine methylsulfate with 0.65 mg. atropine sulfate, to prevent gastrointestinal symptoms, according to the plan devised by Viets.[2] Recently Tether [3] has recommended that the diagnostic test be performed by giving 0.5 mg. of neostigmine intravenously instead of 1.5 mg. intramuscularly. He believes that the intravenous method gives superior results. These tests will result in the abolition of symptoms, or in severe cases their decided amelioration, in from fifteen to thirty minutes by the intramuscular route or in five minutes by the intravenous method. In no other form of muscular asthenia does a response of comparable magnitude occur after the injection of neostigmine. In patients with difficulty in swallowing the correction of the weakness of the pharyngeal muscles by this method can be observed by fluoroscopy of the pharynx in its response to orally administered barium.

Harvey and Whitehill [4] have shown that quinine administered orally intensifies the myasthenic state. This test is especially useful in mild cases, in which it may be difficult to demonstrate classic muscular weakness. As final proof of a diagnosis so established, neostigmine may then be given and its obliteration of the induced asthenia observed.

The great sensitivity of the myasthenic muscles to curare was reported by Bennett and Cash [5] in 1943. They found that one fifth of the usual adult dose of d-tubocurarine chloride would cause an appreciable degree of weakness in doubtful cases. While this method is of value, it should be added that it carries a slight but definite hazard. Again, effects of curare may be reversed by neostigmine. Much safer is the diagnosis arrived at from the history, the physical examination and the response to neostigmine, which seldom fail to provide all the information that is required for complete diagnostic accuracy.

PATHOLOGIC PHYSIOLOGY

The cause of myasthenia gravis is unknown. The observation of collections of cells indistinguishable from lymphocytes, so-called "lymphorrhages," in and about muscle fibers and in other structures, notably the adrenal cortex, has been reported by several observers.[6]

2. Viets, H. R., and Schwab, R. S.: The Prostigmine Test in Myasthenia Gravis: Second Report, New England J. Med. **215**: 1064 (Dec. 3) 1936.
3. Tether, J. E.: Intravenous Neostigmine in Diagnosis of Myasthenia Gravis, Ann. Int. Med. **29**: 1132 (Dec.) 1948.
4. Harvey, A. M., and Whitehill, M. R.: Quinine as an Adjuvant to Prostigmine in the Diagnosis of Myasthenia Gravis: A Preliminary Report, Bull. Johns Hopkins Hosp. **61**: 216 (Sept.) 1937.
5. Bennett, A. E., and Cash, P. T.: Myasthenia Gravis: Curare Sensitivity; a New Diagnostic Test and Approach to Causation, Arch. Neurol. & Psychiat. **49**: 537 (April) 1943.
6. Wilson, S. A. K.: Neurology, London, Edward Arnold & Co., 1940, vol. 2, p. 1601.

Since these cells are not present in all cases their significance is uncertain. Similarly, hyperplasia of the thymus gland and thymic tumors have been observed in about 50 per cent of cases of myasthenia gravis,[7] but the assignment of an etiologic role to dysfunction of the thymus gland, has, as yet, failed to meet critical requirements.

The present concept of the mechanism operative in myasthenia gravis is related to an alteration in physicochemical changes that initiate muscular contraction. It is generally accepted that when a nerve impulse reaches the myoneural junction acetylcholine is liberated, and this substance initiates muscular contraction. Simultaneously, an enzyme, cholinesterase, quickly hydrolyzes the acetylcholine and destroys any further activity. In myasthenia gravis there is an imbalance in the acetylcholine-cholinesterase reaction, so that acetylcholine is prevented from exerting a normal effect. This could result from a decrease in the amount of acetylcholine, an increase in the amount of cholinesterase or other as yet unknown factors. The evidence is inconclusive. Furthermore, the studies of Nachmansohn [8] have indicated that the "acetylcholine cycle" actually consists of a multiplicity of reactions in which the interaction of acetylcholine and cholinesterase is only a part. For the moment we must be content to subscribe to the view that the existence of an abnormal relationship between acetylcholine and cholinesterase gives rise to the weakness and excessive fatigability that characterize this disease. This concept has led to a rational and reasonably satisfactory approach to therapy. It is to be hoped that further laboratory investigation in neuromuscular function will add knowledge that will allow an exact and more detailed understanding of the changes observed in myasthenic patients.

TREATMENT

Prior to the discovery of the profoundly ameliorating effects of neostigmine in myasthenia gravis, treatment of the disease was extremely unsatisfactory, with the consequent high mortality previously mentioned. In 1930 Harriet Edgeworth,[9] herself a victim of myasthenia, reported the beneficial effect of ephedrine sulfate, and even today this drug may at times be profitably employed as an adjunct to neostigmine. Its estimated effectiveness, 10 to 15 per cent that of neostigmine,[10] greatly limits its usefulness. The mode of action of ephedrine is imperfectly understood. It apparently has no action on the acetylcholine-cholinesterase balance but probably acts directly on the tonicity of skeletal muscle. The dose is usually 10 to 30 mg. given orally two or three times daily.

In 1932 Boothby [11] observed that in cases of severe myasthenia gravis there were negative balances for nitrogen, sulfur and phosphorus (as there are in many debilitating diseases). He further showed that there was often a pronounced decrease in creatine excretion. Stimulated by the improvement in the negative nitrogen, sulfur and phosphorous balances and the increased excretion of creatine following the administration of large amounts of the amino acid glycine, he employed glycine in the treatment of patients with myasthenia gravis. In 1936 [12] he stated that the glycine treatment caused "some improvement in nearly all cases and marked improvement in many." Similar results have not been obtained by others, and at present glycine therapy may be regarded only as an interesting historical milestone in the development of current methods of treatment.

Although acetylcholine is the chemical agent that stimulates muscle contraction, it is also known that in some manner potassium ions are concerned with the liberation of acetylcholine, that they may exert a direct stimulating effect and may enhance the action of acetylcholine.[13] On this basis potassium, usually as the chloride or citrate salt, has found its way into the treatment of myasthenia gravis. Wilson and Wright,[14] who in 1927 were the first to suggest the use of potassium, did so on the hypothesis that the ion exhibited a "total decurarizing action." It is generally admitted that potassium salts in doses of 10 to 50 Gm. daily do ameliorate the symptoms of myasthenia gravis, but the effect is seldom sufficient to completely relieve them.

Guanidine hydrochloride has been the subject of investigation in treatment of myasthenia gravis since the publication of a favorable report by Dodd, Riven and Minot [15] in 1938. Guanidine is closely related chemically to creatine and creatinine and has been claimed to possess "a decurarizing action" in myasthenic persons. It is administered in a dosage of 20 to 30 mg. per kilogram of body weight daily in three divided doses. Unquestionable improvement follows in a small percentage of patients, possibly in those showing a low excretion of creatinine,[16] but entirely satisfactory results are so infrequently obtained that there is little justification for its employment.

In 1939 Blalock [17] began an investigative study of the effect of thymectomy in myasthenia gravis. His reports stimulated similar efforts both here and abroad, so that there are now available for analysis well over 100 reported cases in which the operative procedure has been performed. The results are difficult to interpret, because there is complete lack of correlation between the pathologic observations in removed thymus glands and the results on the course of the disease. About 50 per cent of patients appear to have derived benefit from the operative procedure, in that they require less neostigmine postoperatively. A small percentage is reported to be well. Nevertheless, thymectomy is a formidable surgical procedure, patients with myasthenia gravis are poor operative risks and precise indications for the operation are difficult to determine.

The year 1935 marked the beginning of a new and significant era in the study and treatment of myasthenia gravis. This is due to the observation of Mary Walker in 1934 [18] that the muscular weakness of myasthenia gravis is clinically identical with that of curare poisoning. She hypothecated, therefore, that the weakness should be relieved by physostigmine salicylate,

7. Bell, E. T.: Tumors of the Thymus in Myasthenia Gravis, J. Nerv. & Ment. Dis. **45**: 130 (Feb.) 1917.
8. Nachmansohn, D.: Acetylcholine and the Mechanism of Nerve Activity, Exper. Med. & Surg. **1**: 273 (Aug.) 1943.
9. Edgeworth, H.: A Report of Progress on the Use of Ephedrine in a Case of Myasthenia Gravis, J. A. M. A. **94**: 1136 (April 12) 1930.
10. Viets, H. R.: Myasthenia Gravis, J. A. M. A. **127**: 1089 (April 28) 1945.
11. Boothby, W. M.: Myasthenia Gravis: A Preliminary Report on the Effect of Treatment with Glycine, Proc. Staff Meet., Mayo Clin. **7**: 557 (Sept. 28) 1932.
12. Boothby, W. M.: Myasthenia Gravis, in Medical Paper Dedicated to H. A. Christian, Baltimore, Md., Waverly Press, Inc., 1936.
13. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1940, pp. 596-597.
14. Cited by Krantz and Carr,[16] p. 629.
15. Dodd, K.; Riven, S. S., and Minot, A. S.: Further Experience with the Use of Guanidine Hydrochloride in the Treatment of Myasthenia Gravis, Am. J. M. Sc. **202**: 702 (Nov.) 1941.
16. Krantz, J. C., Jr., and Carr, C. J.: Pharmacologic Principles of Medical Practice, Baltimore, Md., Williams & Wilkins Company, 1949, p. 630.
17. Blalock, A.: Thymectomy in the Treatment of Myasthenia Gravis: Twenty Cases, J. Thoracic Surg. **13**: 316 (Aug.) 1944.
18. Walker, M. B.: Treatment of Myasthenia Gravis with Physostigmine, Lancet **1**: 1200 (June 2) 1934.

and a therapeutic trial proved that it was. She then suggested [19] that the analogue of physostigmine, neostigmine, might prove even more efficacious, and it did. Since these reports, numerous studies made in many laboratories and clinics have established a firm foundation for the neostigmine therapy of the disease. It is not an exaggeration to state that the discovery of the effectiveness of neostigmine in this disease accomplished as much for the patient with myasthenia gravis as the discovery of insulin did for the person with diabetes. Not only has it greatly improved the formerly pitiable condition of patients afflicted with the disease, but its advent has stimulated a large amount of chemical, physiologic and clinical research that gives promise of continuing therapeutic progress in myasthenia gravis in particular and in muscular disease in general.

Neostigmine combines with and inactivates cholinesterase. This effect lasts for one to several hours, varying with the severity of the disease. If the dosage is properly regulated as to amount and spacing most patients are able to obtain a more or less continuous remission of symptoms and to lead normal or nearly normal lives. In 85 per cent of cases, oral administration of neostigmine bromide is effective, but in severer disease hypodermic administration of neostigmine methylsulfate—along with the oral dosage—is necessary. In the stage of crisis intravenous neostigmine is indicated and can be given in large amounts, up to 30 or more mg. each twenty-four hours in hourly doses.

However, there are some inadequacies of and disadvantages to neostigmine therapy. Its action is relatively short, it may produce toxic symptoms and it is fairly expensive. In spite of careful regulation of dosage and administration of the drug in large amounts, some patients cannot be completely relieved of symptoms, or their control may be so erratic that normal activities are denied them. For these reasons the search is continued for newer agents that may have fewer objections.

In the past few years three chemical compounds known to have strong cholinesterase-inhibiting properties have been studied: diisopropylfluorophosphate, hexaethyltetraphosphate and tetraethylpyrophosphate. The effect of the first compound has been studied by Comroe,[20] Harvey [21] and others.[22] As a result, it may be stated that this chemical in doses of 2 to 3 mg. administered intramuscularly once or twice a week is capable of exerting a profoundly inhibitory action on cholinesterase, even reducing the plasma level of the enzyme to zero. However, the results in patients are less favorable than those obtained with neostigmine, and unpleasant side effects are encountered much oftener. It is believed, therefore, that diisopropylfluorophosphate is unsuited for the treatment of myasthenia gravis.

Westerberg and Luros [23] reported the trial of hexaethyltetraphosphate (at least 85 per cent of which is tetraethylpyrophosphate [24]) in 4 cases. The drug was given intramuscularly in doses of 10 to 12 mg. every three to five days with resultant improvement. It was impossible to fully control symptoms in any case without the simultaneous use of neostigmine, but the amount of neostigmine required was smaller than when neostigmine alone was used.

Tetraethylpyrophosphate is a colorless liquid miscible with water, acetone, alcohol, glycerin and propylene glycol. It is hygroscopic and is readily hydrolyzed to inert diethyl acid phosphate. For oral administration it is mandatory that the compound be prepared in a form that protects it from contact with moisture. We have found that a 1 per cent solution in anhydrous propylene glycol put up in 10 to 20 cc., tightly capped and waxed, dark glass vials has been fairly satisfactory. It is hoped, however, that there will soon be available either glass ampules or air-tight gelatin capsules of this preparation which will reduce to a minimum the problem of hydrolysis.

In April 1948, Burgen, Keel and McAlpine [25] in England first reported the use of tetraethylpyrophosphate in 3 cases of myasthenia gravis. With administration to the patient of 8 to 12 mg. of the compound per day in two or three divided oral doses they were able to induce complete relief of symptoms. Harvey [26] published the results of his observations in 7 patients treated with the drug in November 1948. He found that the average daily dose of 15 mg. in two or three divided oral doses produced an effect similar to that produced by the optional dosage schedule of neostigmine in the same patients. Maximum depression of plasma cholinesterase occurred within one hour after the administration of the compound, and the relief of symptoms was maximally sustained for twelve hours. After that the effect declined, but a slight depressant effect on cholinesterase continued for as long as sixteen days. Harvey further showed that when neostigmine is given shortly before tetraethylpyrophosphate there is a blocking action on the anticholinesterase action of the latter. In other words, the cholinesterase-neostigmine combination protects the enzyme from the inhibiting action of the compound. This is of importance in the treatment of those patients whose requirements are best served by the combined use of the two drugs. For complete effectiveness, the tetraethylpyrophosphate should be administered one hour or more before the neostigmine.

Stimulated by the English report we have been using tetraethylpyrophosphate for the past year. To date there are 8 patients under treatment. Four patients are now normal; 2 are greatly improved, almost normal, and 2 are classified as moderately improved. The last 2 patients still require some neostigmine; in 1 case 60 mg. a day and in the other 150 to 200 mg. a day. In both instances the current dose of neostigmine is roughly one third of the amount required before the administration of tetraethylpyrophosphate.

Our results have indicated that the full therapeutic dose of this compound is between 13 and 17 mg. per day in two, or occasionally three, divided doses. All anticholinesterase substances produce a characteristic group of toxic symptoms when given in excessive

19. Walker, M. B.: Case Showing the Effect of Prostigmine on Myasthenia Gravis, Proc. Roy. Soc. Med. **28:** 759 (April) 1935.
20. Comroe, J. H.; Todd, J.; Gammon, G. D.; Leopold, I. H.; Koelle, G. B.; Bodansky, O., and Gilman, A.: The Effect of Di-Isopropylfluorophosphate (DFP) upon Patients with Myasthenia Gravis, Am. J. M. Sc. **212:** 641 (Dec.) 1946.
21. Harvey, A. M.; Jones, B. F.; Talbot, S., and Grob, D.: The Effect of Di-Isopropylfluorophosphate (DFP) on Neuromuscular Transmission in Normal Individuals and in Patients with Myasthenia Gravis, Federation Proc. **5:** 182 (March) 1946.
22. Buchthal, F., and Engbaek, L.: On the Neuromuscular Transmission in Normal and Myasthenia Subjects, Acta psychiat. e neurol. **23:** 3, 1948. Gaddum, J. H., and Wilson, A.: Treatment of Myasthenia Gravis with Di-Isopropylfluorophosphate, Nature, London **159:** 680 (May 17) 1947.
23. Westerberg, M. R., and Luros, J. T.: The Clinical Use of Hexaethyl Tetraphosphate in Myasthenia Gravis, Univ. Hosp. Bull., Ann Arbor **14:** 15 (Feb.) 1948.
24. Mangum, G. H.: Personal communication to the author (J.A.R.).
25. Burgen, A. S. V.; Keel, C. A., and McAlpine, D.: Tetra-Ethyl-pyrophosphate in Myasthenia Gravis, Lancet **1:** 519 (April 3) 1948.
26. Harvey, A. M.: Some Physiological Experiments of Nature in the Field of Neuromuscular Function: Tetra-Ethyl Pyrophosphate in the Treatment of Myasthenia Gravis, Potassium Deficiency, Potassium Intoxication, Proc. Inst. Med. Chicago **17:** 182 (Nov. 15) 1948.

amounts. These symptoms are muscle fasciculation, accommodation spasm, miosis, abdominal cramps, diarrhea, lacrimation, perspiration, salivation, nausea, vomiting, restlessness and bradycardia; all are relieved by atropine. Although tetraethylpyrophosphate in too large a dosage gives rise to all these symptoms, as do other agents of similar action, there is one notable difference. In neostigmine toxicity, abdominal cramps are conspicuous, but they are seldom seen in toxic reactions from tetraethylpyrophosphate. In case of toxicity due to the latter compound a bradycardia of 40 was relieved by administration of 0.11 mg. atropine sulfate intravenously, while in another instance a convulsive seizure lasting one minute and followed by a brief period of unconsciousness was promptly relieved by 0.65 mg. atropine sulfate given intramuscularly. In the latter case the pulse rate dropped to 56 per minute and the electrocardiogram showed depressed S-T segments and low voltage of T waves in all leads. These results are similar to those reported by Salerno and Coon [27] in toxicity studies with this drug in dogs.

We have administered the compound in the following manner. In order that accurate dosage prevail, the 1 per cent mixture was withdrawn from the container into a tuberculin syringe just prior to its administration. It was dispensed into a glass of water or milk and given with or shortly after food to avoid nausea and other toxic manifestations. Since most of the patients in our series have previously been treated with neostigmine, we have planned to gradually diminish the amount of neostigmine, and at the same time give increasing doses of tetraethylpyrophosphate, keeping in mind the necessity for giving the drug sometime before administration of the neostigmine. A satisfactory transfer of a patient from neostigmine to tetraethylpyrophosphate may be effected by giving the latter in doses of 2 to 3 mg. with breakfast and supper, that is, at about twelve hour intervals, increasing the amount on the second or third day until a dose of 8 to 12 mg. per day is reached. Neostigmine is allowed meanwhile, according to the need as evidenced by recurring weakness. Usually when a dose of 8 to 12 mg. of tetraethylpyrophosphate is reached neostigmine therapy may be discontinued. From then on, the dosage of tetraethylpyrophosphate is cautiously increased by adding 0.25, 0.5 or 1 mg. daily until there is maximum relief of symptoms without toxic effects. However, we have occasionally observed toxic symptoms as long as three to seven days after the last dosage increase, due to a cumulative effect which necessitated a downward readjustment.

In our experience with this drug the difference between the dose required to produce a maximal response and that which gives rise to toxic symptoms has been within a remarkably narrow range, from 0.5 to 3 mg. This is true regardless of the severity of the disease, duration of the disease, the age, body weight and sex or the previous neostigmine requirement. Since the intensity of symptoms tends to fluctuate spontaneously in patients with myasthenia gravis, it follows that individual adjustment of the dosage of tetraethylpyrophosphate is to be expected. Intelligent and cooperative patients may be taught to do this themselves.

27. Salerno, P. R., and Coon, J. M.: A Pharmacologic Comparison of Hexaethyl Tetraphosphate (HETP) and Tetraethyl Pyrophosphate (TEPP) with Physostigmine, Neostigmine and DFP, J. Pharmacol. & Exper. Therap. **95**: 240 (Feb.) 1949.

Following are illustrative cases of the types encountered in our study.

REPORT OF CASES

Case 1.—W. L., a married Negro woman aged 30, mother of six children, in June 1948 began to have attacks of generalized weakness accompanied with ptosis of the eyelids and difficulty in chewing, talking and swallowing. During August, September and October, 1948, she had several severe attacks of respiratory distress. She was referred to the John Sealy Hospital in November 1948, in the eighteenth week of pregnancy, because she was doing poorly on a regimen of 75 mg. of oral neostigmine daily. Treatment was initially carried out with neostigmine bromide in amounts up to 450 mg. per day. Difficulty in swallowing, generalized weakness and ptosis persisted. The medical regimen was changed to tetraethylpyrophosphate, the required dosage of which was 14 mg. per day in two divided doses. On this regimen she became completely normal. During the last week of pregnancy it was necessary to reduce the dose to 13 mg. per day, because of nausea and vomiting. She was normally delivered of a full term female infant weighing 2,500 Gm. on April 19, 1949. The infant had symptoms of severe myasthenia; inability to nurse, regurgitation of milk through the nose and expressionless facies. These symptoms were promptly ameliorated on the third day by administration of neostigmine methylsulfate 0.07 mg. intramuscularly. Remission was maintained by 2 mg. of neostigmine bromide given orally every three hours for one day, then by 1 mg. every three hours for thirteen days, at the end of which time it was possible to discontinue all medication without return of symptoms. The mother remained normal on a regimen of 13 mg. of tetraethylpyrophosphate daily.

This case is a striking example of one that cannot be completely relieved by treatment with neostigmine; however, a return to a symptom-free status is easily effected by tetraethylpyrophosphate therapy.

Case 2.—O. V., a married white man aged 24, had had myasthenia gravis for eight years and had been treated in the John Sealy Hospital in 1943. Therapy consisted of 90 to 150 mg. neostigmine bromide and 25 mg. of ephedrine sulfate twice daily with incomplete relief, evidenced by a nasal voice, dysphagia, diplopia, ptosis, and postexertional weakness. He was readmitted to the hospital Dec. 8, 1948 and stabilized on 16.8 mg. of tetraethylpyrophosphate per day. His only remaining symptoms were a nasal voice and mild dysphagia. His strength was sufficient for him to do hard manual labor in the oil fields. Subsequently, he has been maintained on 15 mg. of the drug per day with further improvement of symptoms.

This case emphasizes the following points:

1. This patient was unable to afford adequate doses of neostigmine.

2. Relief of symptoms was more complete on tetraethylpyrophosphate than with neostigmine.

3. Although greatly improved, he is not entirely normal.

Case 3.—B. P., a married Negro woman aged 18, noted the development of generalized weakness, ptosis and difficulty in chewing and swallowing in January 1948. She was admitted to the John Sealy Hospital in March 1948. Definite improvement occurred on neostigmine therapy, but despite a daily dose of 1,260 mg. of the drug orally, weakness was so great that she could not walk without holding to her bed. After a six week period of observation, thymectomy was performed, followed by a stormy postoperative convalescence. In the critical period use of a respirator was required and neostigmine methylsulfate in doses as high as 336 mg. intramuscularly in a twenty-four hour period was given. She gradually improved and was put on a regimen of tetraethylpyrophosphate 10 mg. per day with 300 mg. neostigmine orally per day. On this

regimen she could eat well and could walk the length of the ward. She was discharged in June 1948 and was readmitted in October 1948. It was found that she could tolerate 16.8 mg. of tetraethylpyrophosphate per day, but she still had some generalized weakness. At higher dosage levels she had toxic symptoms. Finally it was found that the addition of 60 mg. neostigmine bromide enabled her to be up and around almost at will. She was last seen in the outpatient clinic in April 1949. On this regimen she stated that she could do her housework but could walk only short distances. There was no difficulty with mastication or deglutition.

This case is illustrative of the type that cannot be adequately controlled by either neostigmine or tetraethylpyrophosphate alone but that can be assured a reasonably satisfactory remission of symptoms on combined therapy.

COMMENT

Advances of considerable importance have been made in the understanding and treatment of myasthenia gravis. Yet much remains to be done if there is to be available a complete knowledge of the causes that are operative in disturbing acetylcholine-cholinesterase balance and causing the clinical picture of the disease. A full understanding of all aspects of normal and abnormal muscle metabolism are prerequisite to the solution of the etiologic basis of myasthenia gravis. When this information is available, there will doubtless evolve methods of treatment founded on a firmer basis than current concepts permit.

SUMMARY AND CONCLUSIONS

1. The medical treatment of myasthenia gravis is based on the principle of continuous cholinesterase inhibition at a level consistent with relief of symptoms but without evidences of toxicity. It is a type of substitution therapy and as such must be continued indefinitely.

2. Beyond doubt mild cases, as well as those of greater severity, that can be well controlled with neostigmine (assuming that relatively high cost is not a factor) are best treated with neostigmine.

3. Severe disease and disease of moderate severity in which there is failure to obtain complete relief from neostigmine can be treated with and may be adequately controlled by tetraethylpyrophosphate. In some instances this drug is definitely superior to neostigmine.

4. A small percentage of cases not responding well to either tetraethylpyrophosphate or neostigmine may be stabilized better on combined treatment with the two drugs.

5. The greatest handicap in the use of tetraethylpyrophosphate is the difficulty of adjusting the dose so that complete relief of symptoms is obtained without the production of toxic symptoms, owing to the narrow range that divides the therapeutic from the toxic dose.

6. Atropine is a physiologic antagonist to tetraethylpyrophosphate and should be used if toxic symptoms occur.

7. Ephedrine sulfate, potassium salts and guanidine hydrochloride may occasionally fill the role of helpful supplemental agents to neostigmine or tetraethylpyrophosphate, but seldom does any of the three meet full therapeutic requirements. Glycine is of no value.

8. Thymectomy is still an incompletely appraised procedure which, in our opinion, should be reserved for those cases that defy control by other measures or in which a thymic tumor is known to be present.

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ABSTRACT OF DISCUSSION

DR. DAVID GROB, Baltimore: We have had an opportunity to administer tetraethylpyrophosphate to 12 myasthenic patients for periods up to one year, and our conclusions have been in general similar to those of Dr. Stone. Six of our patients were able to tolerate the compound and have preferred this drug to neostigmine because of the prolonged increase in muscular strength which it provides throughout the day and night. However, although the increase in muscular strength has been more prolonged after tetraethylpyrophosphate than after neostigmine, the maximum degree of motor power has usually been about the same after both of these compounds. In general, muscles that have responded poorly to neostigmine have also responded poorly to tetraethylpyrophosphate, and to this drug followed by neostigmine. Six patients were unable to tolerate tetraethylpyrophosphate. In 4 there developed moderately severe muscarinic and central nervous system symptoms which could not be fully controlled by large doses of atropine, while profound muscular weakness developed in 2 after an overdose of tetraethylpyrophosphate. This effect of an excess of anticholinesterase agent resembles the effect of anticholinesterase agents in normal subjects and was also seen in 3 myasthenic patients who received neostigmine while they were at maximum strength after tetraethylpyrophosphate therapy. In contrast, when neostigmine was administered at a time when the strength was below maximum, subsequent to tetraethylpyrophosphate, the effect of the neostigmine was usually potentiated. Although the ability of the former drug to restore power to myasthenic muscles bears a general resemblance to the effects of the latter, certain differences must be noted, in addition to the more prolonged action of tetraethylpyrophosphate. A large initial dose of this drug, about three times the daily maintenance dose, is required before its physiologic effects are produced, and if the maintenance dose is omitted for several days a large initial dose must again be given. The range of effective maintenance dose of the agent between that which produces no observable effect and that which causes distressing symptoms is exceedingly narrow. Extreme caution is required in the regulation of myasthenic patients with tetraethylpyrophosphate. It appears to exert its effects by depressing the cholinesterase activity of the tissues below a threshold at which changes in function begin and by maintaining this degree of depression. These characteristics of the action of tetraethylpyrophosphate are in contrast to those of neostigmine and suggest that there may be a qualitative as well as a quantitative difference in the mode of action of these compounds.

DR. CHARLES T. STONE, Galveston, Texas: I am in agreement with most of the points made by Dr. Grob, some of which have been discussed in the paper. I should like to emphasize two of the important toxic effects of tetraethylpyrophosphate, which are dramatic and which may be serious. The first of these is bradycardia, which, if sufficiently severe, may cause symptoms similar to those occurring in complete auriculoventricular dissociation. The second is convulsive seizures of an epileptiform type, which occurred in 1 of our cases. Fortunately, these severe symptoms are promptly relieved by the intravenous administration of atropine. In the electrocardiogram the toxic manifestations may be evidenced by depressed S-T segments and low voltage of T waves in all leads. These observations are identical with those reported by Coon of the University of Chicago in his toxicity studies with tetraethylpyrophosphate in dogs. Situations of this nature demand that the utmost caution be exercised in the employment of this drug until some of the difficulties incident to its use have been eliminated. Tetraethylpyrophosphate is powerful and dangerous. Its use to date has extended slightly more than a year, and only a relatively small number of patients have been treated with it. Therefore it is still in the experimental stage and should not be employed unless one is cognizant of the difficulties that may develop incident to its administration and unless measures are immediately available for the correction of toxic symptoms which it may produce.

THE PREPSYCHOTIC AND EARLY PSYCHOTIC SEE THE FAMILY PHYSICIAN OR INTERNIST FIRST

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The reduction of the enormous amount of personal and social suffering due to psychoses is an urgent medical challenge. We have left to psychiatrists, pitifully few and all too inadequate in terms of needs, this major problem of human sacrifice. The coming generation of physicians may include in their armamentarium an understanding of psychodynamics. It might be well for the rest of us to arouse enough interest in the psychoses to give our patients a modicum of understanding. Anything less may produce a dangerous scotoma.

Regardless of his interests, no physician is immune from contact with psychoses. The doctor who complacently refuses to be concerned may find himself appealing for help when his aged father experiences hallucinations, his postpartum patient obeys a command over the radio to jump out of the window or the patient on whom he refused to perform a surgical operation enters the office with a .38 automatic in his hand.

Even the clinical pathologist may be called on to make repeated serologic tests for syphilis by a self-accusatory, depressed patient.

H. L. took his four children across a street for ice-cream cones. The daughter, 3 years of age, ran in front of a car and was killed. Shortly thereafter the patient became depressed and unable to work. His mind turned to a sexual dereliction of a year previous, and he became obsessed with fear of a venereal disease. He visited a number of physicians and laboratories for blood tests, all of which gave negative reactions, and he finally interfered with his wife's housework by constantly demanding that the whole family go to the laboratory for tests. Fortunately the next internist who saw him arranged for a successful course of electric shock treatments.

Study of the evolution of psychoses, particularly with analytic methods, has helped to elucidate the mechanism by which the distorted thought processes take place. Perhaps of even greater practical value is the contribution of child development studies, examining the effect of continuous personal, family and school pressures. Those who have been searching for a single traumatic event to explain the patient's psychopathology may well look for these continuous pressures instead. The impact of watching the primal scene, an event so cherished by the analysts, may have less effect on the child than the way his mother is greeted by his father after a hard day at the office.

Somewhere in the course of the psychoses must be a stage where we can increase our influence for the good. When the onset is abrupt, the patient may fall into psychiatric hands rapidly, but too often an insidious onset may involve the patient with the family physician, unsatisfactorily, for months or years. Unfortunately, many members of the medical profession think of psychoses in terms of deteriorated schizophrenic persons in the back wards of state hospitals, not remembering that such is the end result of a process which might have been controlled had it been recognized earlier.

Popular impression is that shy, withdrawn, daydreaming children are more apt to become schizophrenic than are aggressive, out-going, active children. This may prove to be a myth.

The first warning sign often occurs as an adolescent failure of socialization. The major break with reality may come at the time of facing new sexual, social or economic responsibility. Probably 5,000,000 subclinical schizophrenic subjects live in society without major friction; often they are obscure persons in small jobs, nursing some particular maladjustment, on the fringe of reality, for the most part keeping out of trouble.

For the 300,000 schizophrenic persons who have broken overtly with reality and are confined to designated hospitals, we are obliged to be alert for possible contributions from medical science.

With those entering the psychoses (schizophrenia takes an annual toll of 150,000) we are more directly concerned, for many of them will seek help from physicians; hence, the first opportunity and responsibility for appropriate diagnosis and guidance into proper hands lies with us. The presenting symptoms often lead the patient to the doctor's office and the doctor on a futile chase until the basis for the symptoms is discovered in the psychic structure of the patient. Among these symptoms are those due to excessive awareness of physiologic activity, disturbed interpretation of physiologic activity and disturbed physiologic activity due to alterations in the central integrative levels of the autonomic nervous system.

In our society a person with disturbed ideas and physical symptoms visits the physician for relief of his symptoms. Despite our apparent sophistication, ideas of demonic possession, punishment for sin (of the patient or his forebears) or moral weakness pervade our concepts of mental disease. And there is a prevalent willingness to attribute all physical symptoms and even behavior and personality problems to lack of vitamins, or nutritional anemia. Even though the patient's thoughts or behavior are so bizarre that he or the family may realize the need for psychiatric attention, the physician is usually consulted first. Organic disease is, for the most part, socially acceptable —mental disease is not. Going to the family physician or medical specialist carries social approval and may even be a prestige-seeking measure. A visit to a surgeon even carries glamor. But any one who goes to a psychiatrist "must be nuttier than a fruit cake."

Particularly in depressions are the physical changes apt to be prominent: loss of weight, anorexia, digestive difficulties, weakness, fatigue, sleep disturbances, aches and pains, altered sexual and menstrual functions. Hence the symptoms lead the patient to the family physician. If a specialist is sought, the symptoms are of a nature most apt to fall in the field of the internist (as contrasted to the acute, dramatic symptoms of the hysterical patient, often referred to the surgeon).

In many communities, and even in one whole state, there are no psychiatrists in private practice, hence the physician may be the only "psychiatrist" available.

The history taking of prepsychotic or early psychotic patient is an interesting experience. In the schizophrenic person the difficulty in communication soon becomes obvious. By ordinary standards the history may be vague, confused and fragmentary, a maze of minor flights without a central theme. But the very nature of the history may be the best diagnostic

From the Salt Lake Clinic.
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clue to the disordered thought processes. The history of a depressed patient may be an endless list of complaints. Attention to the way the patient feels about each complaint is often a valuable clue, as is the observation of the behavior of the patient during the interview.

The question and answer type of history is less valuable than an effort to draw out the history of the patient with sympathetic, interested encouragement. Certain questions often have to be asked, particularly about hallucinatory experiences, thoughts of suicide or ideas of reference or influence. Direct, blunt questions, as "What are the voices saying?" may impair an already tenuous rapport.

A few moments with a responsible relative of the patient may be enlightening.

The physical examination may be sterile of results, except in those psychoses with associated organic disease, yet a neglected, incomplete or sketchy physical examination is a serious mistake. The patient's behavior during the examination may be of utmost importance.

Since both the history and physical examination are time consuming and somewhat subjective, there may be a temptation to skip over both as rapidly as possible, and, like the fat man in the art gallery who brushes the attendant aside and asks, "where are the nudes?" the physician may exhibit premature interest in the "scientific" disciplines.

A relatively small percentage of patients have psychoses diagnosable by laboratory methods, but those should not be overlooked (particularly bromide intoxication), and fewer by roentgenologic methods (e. g., the psychoses often associated with post-traumatic subdural hematoma).

If we depend unduly on laboratory diagnosis we may find some slight deviation from normal of the white blood cell count, the alkaline phosphatase or the blood rhubarb titer. And if the diagnosis and regimen of therapy are unsuccessful in relieving the psychotic symptoms, we are apt to make repeated excursions through the laboratory, the x-ray office or the pharmacopeia, the patient winding up with his psychosis intact, a fixation that the condition is organic (even if undiscovered), with a stack of roentgenograms, a sheaf of laboratory reports, a pocketful of bills, a firm appreciation of the high cost of medical care and an appointment with a chiropractor.

Certain clues, although not diagnostic of schizophrenia, may serve to heighten our suspicion:

1. Inability to communicate—the feeling of talking at the patient, not to him.

2. A list of symptoms that fall through the grasp like water from a sieve, or a list of symptoms so bizarre that no one syndrome could explain all of them and no one organ could be capable of so much mischief.

3. Frequent failure of the patient to convey an adequate or entirely plausible reason for the visit. If pinned down by the detective where-do-you-hurt interrogation, he may dwell on some minor ache or pain as a face-saving device, or may actually invent a pain and then himself believe that it exists. Or he may be preoccupied with his own thoughts or sensory misinterpretations.

4. Suggestions of reference or influence—the patient is being forced against his will to do or think certain things. He may be suspicious, and concerned over dictaphones or harmful "rays" from an air-conditioning unit.

5. Behavior out of context of the situation—laughter while discussing the cause of the father's death, or tears while discussing dietary habits, or odd posturing, grimacing or repeated mannerisms.

6. Resistance—as one patient said to his mother, "You can make me go to the doctor, but I won't tell him anything." (He can't have any of my precious thoughts.)

7. Excessive concern over abstract problems, social, religious or philosophical issues, or exaggeration of self esteem.

8. Difficulties in emancipation from a parent—a mother bringing in a son 24 years of age is a frequent clue.

Certain depressive signs are easily seen:

1. A depressed, "sour-puss" demeanor. The patient may try to be pleasant and gay, only to burst into tears unexpectedly.

2. Restless agitation—wringing the hands or repeated stroking of the body, or demanding that the accompanying relative "take me home."

3. An endless "organ recital" of complaints—especially those centering around the narcissistic areas, the head and the pelvis.

4. Blocking, reluctance to talk about, or excessive emotional responses to thoughts of certain events—such as the woman who, two years after the death of the husband, continues to talk of nothing else and cries whenever she talks of it.

5. Ideas of sin, of guilt, of punishment or of influence by supernatural evil personages. Often the patient in a depression searches his past life and tries to assign a causative role to any previous indiscretion or defection, real or fancied.

6. Somatic symptoms, often simulating carcinoma.

7. Reference to self destruction. The truly depressed person may be quite sincere and serious, and his warning may be an appeal for help.

SUMMARY

In our culture, the psychotic patient in the incipient and early stages first seeks help, voluntarily or by coercion, from the family physician or the internist. Dissection of the case into the presenting physical complaints often leads the doctor to a series of misplays: repeated examinations, will-o'-the-wisp excursions through the x-ray department and the laboratory, running tours through the pharmacopeia or attack on various inoffensive organs with a scalpel. Evaluation of the total symptom constellation in terms of the patient's personality often permits an early psychologic diagnosis in the stage where treatment is most efficacious.

115 East South Temple Street.

ABSTRACT OF DISCUSSION

DR. HERBERT F. ROBB, Belleville, Mich.: Specialization often creates problems much like a jigsaw puzzle, in which it is not always easy to fit the parts in their proper position to complete the picture. The patient's reaction to his environment shows a decided variation, depending on whether he is physically and mentally fit, and this varies to a degree with the adequacy of the diet. Vitamin B_1 is essential for the complete combustion of carbohydrates. In cases of vitamin B_1 deficiencies, combustion is arrested at the stage of pyruvic acid, which is not efficiently utilized by the brain, the nervous system or the heart. The person is often easily fatigued, irritable and sensitive; he objects to suggestions or criticisms and does not think or associate ideas clearly. If a child develops from 10 to 18 years of age with a continuous or intermittent thiamine hydrochloride deficiency, and is unable to take suggestions or to adjust himself properly to an ever changing environment, there too often develops a personality with an adult body, but a child's understanding of social and economic problems. Many cases of adolescent delinquency and adult confusion could have been prevented or frequently relieved by a few injections of thiamine hydrochloride, if given before the development of long-established attitudes, conditioned reflexes and structural changes. Thiamine hydrochloride therapy, of course, is of value only in cases of deficiencies and cannot

compensate for the long-continued, devastating influences of an irrational and emotional environment. In our machine age there is greater mental conflict (with normal biologic and reproductive expression opposed by mental, economic and moral restraints) than existed or does exist in an agricultural environment. Leisure time and unemployment of youth as a result of the use of machines and mass production have created a problem which our educational institutions assume to solve by occupying youth with competitive sports and recreation. We have failed to prevent an increase in psychoses and economic social and political problems because in an age of specialization we fail to adjust the individual and society to the new physical, economic, social, moral and political problems of living in our rapidly changing world.

DR. LOUIS G. MOENCH, Salt Lake City: In the last ten years word has gone out from the teaching centers that neuroses are the concern of all physicians. We are trying now to add that the psychoses are also the concern of all physicians. Just as the surgeon likes to treat the patient with appendicitis before peritonitis sets in, just as the internist likes to treat the patient with a failing heart before the stage of decompensation sets in, the psychiatrist likes to treat the psychotic patient before he is climbing up and down the walls. Yet, the psychiatrist is in an odd position. He seldom sees the patient in the early stages; hence, he often has to resort to the drastic therapies of insulin or electric shock or lobotomy, which are probably the most primitive of all medical treatments in this day and age. It is hoped that eventually the physician can dispense with such forms of treatment if he can treat these patients in the early stages.

HEALED SUBACUTE BACTERIAL ENDOCARDITIS, A NEW ENTITY

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Subacute bacterial endocarditis has been, until recently, an almost uniformly fatal disease. Statistics relative to the mortality in the prepenicillin era have varied from practically 100 per cent as quoted by most observers [1] to 97 per cent noted by Libman.[2] Because of this poor prognosis, the major effort in the past has been directed toward obtaining more effective forms of therapy for the eradication of the infection. Until recently relatively little attention could be devoted to the long-term influence of the infectious process on the myocardium, valvular apparatus and previous cardiovascular abnormalities, because so few patients survived the active phase of the disease. With the advent of more successful therapy, a cure of the active infection has been achieved in a significant number of cases, and greater therapeutic success can be anticipated as the methods improve. Unfortunately, in the entity of healed subacute bacterial endocarditis increasing examples of a new complication are appearing. These patients represent a previously unanticipated course of events: with adequate therapy complete arrest of the infection has resulted, but damage sustained by the heart before the disease was brought under control has contributed to the deterioration of the patient through the development of congestive heart failure. What is the nature of the permanent cardiac damage, the residuum of the controlled infection? Pertinent systematic follow-up studies of these cases are now becoming possible, and recently several isolated reports have appeared relative to this question.

This report concerns the subsequent course of a group of 18 patients whose subacute bacterial endocarditis was treated and whose active infection was cured at the Michael Reese Hospital during the years 1944-1947. The minimum follow-up period is twenty-five months, the maximum sixty-one months. Fifteen of these patients have been previously reported in discussions of the treatment of subacute bacterial endocarditis with penicillin [3] and 3 have been subsequently added. Conclusive clinical evidence and at least two positive blood cultures in our own laboratory were obtained in every case before treatment was begun. In 12 instances the infection was engrafted on rheumatic heart disease and in the remaining 6 on a congenital lesion. The duration of illness prior to treatment varied from three to forty-two weeks. The causative organism in all but 1 case was Streptococcus viridans, the exception being a beta-hemolytic Streptococcus. Treatment was based on the in vitro sensitivity of the causative organism and especially on the clinical results. The total dosage of penicillin varied from 3.6 to 151 million units, and the total hospital stay from eighteen to one hundred and forty-five days.

Follow-up studies were made after discharge of the patients from the hospital at intervals of six months. An interim history, physical examination, fluoroscopic study and roentgenograms of the chest, blood culture and electrocardiogram were obtained at almost every visit. There was no instance of recurrence of the disease.

ANALYSIS OF CASES

On the basis of our follow-up study the series is divisible into two groups.

GROUP 1.—*Progressive Heart Disease*

This group consists of those patients whose subsequent progress, it is felt, was affected by the course of the subacute bacterial endocarditis. Roentgenographic, electrocardiographic and clinical evidence of progressive heart disease was revealed in all 6 patients who fell into this category. These have been further subdivided as (*a*) dead and (*b*) living.

(*a*) Dead: Three patients have died in congestive heart failure eight, nine and thirty-nine months, respectively, after the cure of their infection. In none of these was there evidence of cardiac failure before the onset of the endocarditis. The single common factor is a dynamically severe aortic regurgitation, viz: a regurgitation causing not only a diastolic aortic murmur but also a wide pulse pressure, Corrigan's pulse (water-hammer pulse), pistol-shot femoral pulses and definite evidence of strain on the heart.

(*b*) Living: The 3 patients in this group have exhibited definite evidence of progressive heart disease

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This article has been abbreviated in THE JOURNAL by omission of the tabular data, which will appear in author's reprints only.
Acknowledgement is made of assistance by various members of the department in the follow-up observations, and by the physicians who have cared for these patients.
From the Cardiovascular Department (supported in part by the Michael Reese Research Foundation), the Medical Research Institute and the Department of Medicine, Michael Reese Hospital.

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3. (*a*) Grossman, M.; Feldman, D.; Katz, L. N., and Brams, W.: Treatment of Subacute Bacterial Endocarditis Due to Organisms Highly Resistant to Penicillin, Am. Heart J. **34**: 592, 1947. (*b*) Mokotoff, R.; Brams, W.; Katz, L. N., and Howell, K. M.: The Treatment of Bacterial Endocarditis with Penicillin, Am. J. M. Sc. **211**: 395, 1946.

since discharge from the hospital, although congestive heart failure had not been previously discernible. Two of these patients (cases 5 and 6) display the same severe aortic insufficiency that was present in the patients who died of heart failure. The third (case 4) shows a combination of a patent ductus arteriosus and diastolic aortic murmur dynamically akin to the conditions observed in the preceding patients. A decidedly increased pulse pressure is present in this last patient and cardiac catheterization studies have demonstrated the ductus to be one of large size. The net result is a heavy increase in the load of the left ventricle.

Thus, of the 18 patients, 6 have shown definite alteration of their clinical course attributable to the after-effects of subacute bacterial endocarditis. In 3 the effect has been severe enough to lead to death from congestive heart failure. The single important lesion present in all 6 of these cases is a dynamically significant aortic regurgitation. In 5 instances the underlying lesion was that of acquired heart disease.

GROUP 2.—*Without Aggravation of Cardiac Status*

This group includes 12 patients in whom subacute bacterial endocarditis apparently appeared as an ordinary intercurrent infection. There is no evidence that the healing of the infection has aggravated the preexisting cardiac disease. In 3 instances an aortic regurgitation murmur is present but without other observations to indicate that it has important dynamic significance. In 7 of the 12 cases the underlying lesion is rheumatic heart disease. There are 4 instances of interventricular septal defect and 1 classified as miscellaneous.

Thus 12 of the 18 patients have revealed no significant change in their cardiac status in spite of the existence of healed subacute bacterial endocarditis. In none of these is there a dynamically significant aortic incompetence, although acoustic [4] aortic regurgitation is present in 3 patients.

COMMENT

It is a common experience in clinical medicine that with the addition of new weapons to the armamentarium, concomitant new obstacles may appear. As early as 1945 reports were appearing of deaths due to congestive heart failure in patients who had been treated and cured of the active infection in subacute bacterial endocarditis. Rosenblatt and Loewe [5] cited 2 cases, Bloomfield and Halpern [6] another and Flippin and his group [7] an additional 3. In subsequent years other reports appeared by Honigman and Karns,[8] Dawson and Hunter,[9] Glaser and co-workers,[10] Jones and his colleagues,[11] Solomon and Grayzel,[12] Herring and Davis [13] and Christie.[14] In reviewing these reports one is distressed to note that in too many instances the cardiac status prior to the endocarditis was relatively good and, barring the infection, unlikely to lead to so early a death of the patient.

With longer periods of observation, there have been attempts to correlate other factors in the illness with progressive cardiac disability after cure of the active endocarditis. Thus Rapoport and Ellis [15] were unable to find any correlation in their series between the development of cardiac failure and either the duration of illness or the age of the patient. Jones and his group [11] have indicated that the longer the duration of illness the more pronounced is the cardiac enlargement and the renal involvement, and the more frequent is heart failure and uremia. They could find no correlation between the severity of the cardiac damage before the infection and the mortality or between age and mortality in the younger age groups, although all patients over 50 in their series died. Fiese [16] reviewed 25 cases of penicillin-treated subacute bacterial endocarditis which had been followed for three to twenty-five months. Although cardiac efficacy after treatment seemed to be determined mostly by heart size and reserve at the time treatment was begun, no one of the following factors—the patient's age, the type of heart disease, the clinical appearance and the height of the temperature—could be correlated with the subsequent course. In a review of 269 cases of penicillin-treated subacute bacterial endocarditis Christie [14] recently found no correlation between prognosis and age, whereas the existence of heart failure before treatment was of extreme importance. Although he stated that the primary cardiac lesion appeared to be of little significance, the highest death rates were found in those patients with aortic valve defects, whether congenital or acquired.

Our study, too, has revealed no correlation between progressive heart disease following cure of the endocarditis and age, sex, duration of illness prior to treatment, length of hospital stay or total penicillin dosage. Rather, it has become apparent to us that the presence of a dynamically significant aortic insufficiency is the common factor in our patients with progressive cardiac disease. This is reminiscent of the progressive nature of syphilitic aortic regurgitation. Contrariwise, in not a single case in which there was no progression of the previous cardiac status was dynamic aortic insufficiency present, although it was noted acoustically in 3 cases. It is interesting that, of Jones's [11] 29 patients with underlying rheumatic heart disease 16 had aortic incompetence, 10 with development of congestive heart failure. In 2 others aortic insufficiency subsequently developed and congestive failure followed. In striking contrast is the fact that cardiac insufficiency was noted in only 2 of 11 patients without aortic regurgitation. Furthermore, both of the deaths reported by Glaser [10] were in patients who had aortic incompetence, and of the 2 additional (living) patients with congestive heart failure 1 had aortic insufficiency. The 1 death cited by Dawson and Hunter [9] was due to congestive heart

4. Acoustic aortic regurgitation is that type in which the diastolic murmur is unaccompanied by other important observations noted in dynamic aortic insufficiency: namely, wide pulse pressure, water-hammer pulse, pistol-shot femoral pulses and changes in the left ventricle due to the increased strain.

5. Rosenblatt, P., and Loewe, L.: Healed Subacute Bacterial Endocarditis, Arch. Int. Med. **76:** 1 (July) 1945.

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9. Dawson, H. M., and Hunter, T. H.: The Treatment of Subacute Bacterial Endocarditis with Penicillin, Ann. Int. Med. **24:** 170, 1946.

10. Glaser, J.; Smith, R. O.; Harford, C. G., and Wood, W. B., Jr.: The Treatment of Bacterial Endocarditis with Penicillin, J. Lab. & Clin. Med. **31:** 291, 1946.

11. Jones, A. M.; Herring, R.; Langley, F. A., and Oleesky, S.: The Penicillin Treatment of Subacute Bacterial Endocarditis, Brit. Heart J. **9:** 38, 1947.

12. Solomon C., and Grayzel, D. M.: Recovery from Subacute Bacterial Endocarditis (Case Report), Am. Prac. **3:** 564, 1949.

13. Herring, A. C., and Davis, W. M.: Penicillin Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **138:** 726 (Nov. 6) 1948.

14. Christie, R. V.: Penicillin in Subacute Bacterial Endocarditis, Brit. M. J. **1:** 1, 1948.

15. Rapoport, B., and Ellis, L. B.: The Effect of Subacute Bacterial Endocarditis on the Course of the Underlying Heart Disease, New Eng. J. Med. **239:** 951, 1948.

16. Fiese, M. J.: Cardiac Failure in Penicillin-Treated Subacute Bacterial Endocarditis, Arch. Int. Med. **79:** 436 (April) 1947.

failure with aortic regurgitation. The same was true of the cases of Rosenblatt and Loewe,[5] Honigman and Karns,[8] Herring and Davis [13] and Solomon and Grayzel.[12] The single death in heart failure associated with mitral stenosis, reported by Bloomfield and associates,[17] stands out in sharp contrast. This aortic insufficiency of subacute bacterial endocarditis is physiologically identical with that of the progressive varieties of uncomplicated rheumatic or syphilitic aortic regurgitation. With each increment of progression of the lesion a disproportionately greater stress is placed on the left ventricle. Finally, when congestive failure intervenes it is almost totally irreversible.

Thus the compilation of previous experiences, coupled with our own, adds an important prognostic tool to the changing approach to subacute bacterial endocarditis. The presence of a dynamically significant aortic insufficiency, following cure of the infection, definitely curtails the predictable life span. Furthermore, it is important to recognize and treat this disease early, in order to abort as soon as possible the action of both the extremely destructive and the smoldering type of organism, notwithstanding the fact that statistically the duration of illness correlates poorly with the ultimate course of the disease. Besides progressive aortic regurgitation, acute rheumatic fever can recur in patients with healed subacute bacterial endocarditis; and in the elderly patients progressive coronary disease can add to previous cardiac damage.

Of basic importance is the question whether penicillin plays any part in the development of progressive heart disease. In the prepenicillin era unmistakable evidence of healing was seen in all but the most acute cases side by side with more or less active or inactive infection. So accustomed was the pathologist to seeing this strong tendency toward healing that he was led to remark, "If only the patient had lived a little longer he would have recovered." [1] Pathologic observations similar to those in recent cases were noted in the spontaneously cured patients reported by Libman.[2b] Furthermore, tabulation of the incidence of congestive heart failure in the prepenicillin era by Fiese [16] and by Buchbinder and Saphir[18] was approximately 80 per cent. These figures were determined on terminal or moribund patients. In contrast to this is the incidence of congestive heart failure in only 30 per cent of penicillin-treated patients in Fiese's series,[16] 40 per cent in Christie's[14] analysis and 16.5 per cent in ours. Thus, it seems that penicillin not only serves the function of tiding the patient over his illness through additional bacteriostatic and bactericidal action but actually, by checking the thromboembolic "showers," is a factor in reducing the incidence of cardiac insufficiency. Apparently it is only when the progressive increase in aortic regurgitation occurs as part of healing that it dynamically upsets the usual trend.

Finally a brief reference must be made to the myocardial and endocardial pathologic processes in subacute bacterial endocarditis. From a number of excellent reviews it can be concluded that both the initial lesion and the healing process are identical in the treated and untreated patients. Differences lie only in the stages of healing. Healing is more advanced in those patients receiving penicillin and retarded in those patients unexposed to it. This has been aptly stated by Hildebrand and Priest [19]: "In patients treated with penicillin, the lesions of subacute bacterial endocarditis revealed marked evidence of healing. . . . The healing process itself is the same as that presented in standard textbooks of pathology except that the process is more advanced in patients treated with penicillin, and acute inflammatory reaction is much more marked than is described in the medical literature to date." It is in this healing that the detrimental hazard lurks.

17. Bloomfield, A. L.; Armstrong, D. C., and Kirby, W. M.: The Treatment of Subacute Bacterial Endocarditis with Penicillin, J. Clin. Investigation **24**: 251, 1945.

18. Buchbinder, W. C., and Saphir, O.: Heart Failure in Subacute Bacterial Endocarditis, Arch. Int. Med. **64**: 337 (Aug.) 1939.

SUMMARY

1. Eighteen cases of penicillin-treated and cured subacute bacterial endocarditis have been followed for twenty-five to sixty-one months following discharge of the patient from the hospital.

2. Six patients (one third) have shown progressive cardiac disability since the onset of the endocarditis. In 3 the disability was so severe as to lead to death from congestive heart failure eight, nine and thirty-nine months, respectively, after cure of the infection. The single common factor in all 6 of these patients is dynamically significant insufficiency of the aortic valve, which led to strain of the heart.

3. Twelve patients have shown no progression of their cardiac status in spite of the existence of healed subacute bacterial endocarditis. In none of these is there dynamic aortic insufficiency, although acoustically it was noted in 3 instances.

4. No correlation can be found between progressive cardiac disability following cure of the infection and age, sex, duration of illness prior to treatment, length of hospital stay or total penicillin dosage.

5. The significance of penicillin in the development of progressive heart disease is discussed.

19. Hildebrand, E., and Priest, W. S.: Cardiac Lesions in Subacute Bacterial Endocarditis Treated with Penicillin, Am. J. Clin. Path. **17**: 345, 1947.

Authors-Doctors.—There are many instances of distinguished authors being doctors, men drawing upon their knowledge of the frailties of human nature to illumine the theme of their books. One of the best examples is Tobias Smollett, an irascible Scotch doctor, who discovered Nice and the Riviera for us and the French. Then, we have Sir Thomas Browne (1605-1682), the beloved physician, who despite the civil war raging around him sat placidly writing the RELIGIO MEDICI. If you want confirmation of his genius and charm of style, take up and read the concluding chapters of URN BURIAL. Tchekow, the Russian, is another doctor who had enormous influence on his generation, his greatest masterpieces perhaps being THE DUEL, WARD NO. 6 and THE BISHOP. It is hardly necessary to recall to you Conan Doyle of Sherlock Holmes fame; Somerset Maugham, that master of drama and the short story; Brett Young and Warwick Deeping. . . . These are names known to all, but I wonder how many realize that Clemenceau, The Tiger, and President of the French Republic, was a practising physician throughout his long life, nor must we forget that Robert Bridges, the Poet Laureate, was a cultured physician, many of whose poems show the soul and instinct of an artist alive to human suffering. Sir Charles Wyndham, perhaps one of the most beloved men of our stage, was a surgeon in the American Civil War and often gave to his audience the benefits of his medical knowledge.—V. B. Green-Armytage, M.D., The Debt of the Fine Arts to Medicine, *Cambridge University Medical Society Magazine*, Easter term, 1949, Reprinted from "The Embryo," Summer, 1947.

RENAL FAILURE ASSOCIATED WITH LOW EXTRACELLULAR SODIUM CHLORIDE

The Low Salt Syndrome

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In an earlier report [1] attention was called to a condition seen in 2 patients with congestive circulatory failure [2] and diminished renal function. When the intake of fluids was rapidly increased, urinary volume did not increase proportionately and dilution of electrolytes in extracellular fluids occurred. Besides gain in weight there was oliguria and retention of nitrogen in the blood; patients complained of weakness, drowsiness and muscular cramps and became prostrated. It was believed that this sequence of events represented "water intoxication" resulting from a high intake of water and a low intake of salt.

Further experience with this condition has since accumulated. It developed in over one third of a series of 40 cardiac patients being studied. It was precipitated not only by excessive intake of fluids but more commonly by the overenthusiastic use of mercurial diuretics in conjunction with diets low in sodium chloride. It has developed spontaneously when arterial hypertension was treated by salt restriction.

The use of dextrose solutions for postoperative care, without adequate replacement of losses of electrolytes, has sometimes resulted in similar states of renal insufficiency. When large amounts of sodium chloride were lost from the body by other routes (as, for example, by biliary fistulas), oliguria or anuria often developed. In fact, any situation which caused a low concentration of sodium and chloride in extracellular fluids, regardless of the total amount of such fluids, appeared to predispose already disturbed kidneys to a depression of renal function, with consequent oliguria and retention of nitrogen in blood. The presence of shock was not a necessary component of this condition, nor was a state of acidosis or alkalosis, carbon dioxide–combining power of the plasma being usually within the normal range. With the wide employment of low salt diets in congestive failure and hypertension and with the often excessive use of dextrose in water for postoperative care, renal insufficiency from this cause may be more frequently observed. As it usually is unrecognized unless looked for specifically, and as adequate replacement therapy will often alter an otherwise fatal outcome, the present report will describe 21 cases of the condition and methods for its treatment. The term "low salt syndrome" is suggested.

SIGNS AND SYMPTOMS

The development of the low salt syndrome was recognized by (1) a successive depression of urinary volume occurring during three to five days; (2) a depression of urinary chlorides to negligible quantities (which did not increase after injection of mercurial diuretics); (3) a rapid progressive gain in body weight; (4) an elevation of the nonprotein nitrogen content of the blood; (5) a fall in the plasma levels of chloride and sodium,[3] and (6) occasionally an elevation of the cardiac rate.

Symptoms of which patients complained were (1) drowsiness, weakness and lethargy (often wrongly attributed to sedatives), (2) loss of appetite sometimes with thirst, (3) nausea and occasional vomiting, (4) occasionally abdominal or muscular cramps and (5) the secondary symptoms of an increase in extracellular fluids when edema was already present.

In every case observed so far there was evidence either of some degree of organic renal disease, usually without renal insufficiency, or of a functional renal disturbance such as that associated with congestive failure. In chronic glomerulonephritis with moderate renal insufficiency a similar situation often developed. Although spontaneous recovery sometimes occurred, partial renal shutdown usually persisted until death. Reversal of the process as soon as it was detected was considered important; permanent functional changes probably occurred as the condition became established, against which treatment was often useless.

TREATMENT

Therapy was aimed at rapid restoration of the concentration of sodium and chloride in extracellular fluids to relatively normal levels by intravenous injection of hypertonic solution of sodium chloride (5 or 6 per cent). The rationale was as follows:

1. The whole extracellular fluid mass contained an amount of sodium chloride insufficient to maintain normal osmotic equilibrium. Probably intracellular fluids were increased. The net result was overhydration.

2. The most rapid method of restoring the concentrations of sodium and chloride to normal was to administer salt without water. Any water given would decrease the increment between the concentration of salt introduced into the body and the concentration present in extracellular fluids. For example, if body fluids contain a concentration of 75 milliequivalents per liter of chlorides and 120 milliequivalents of sodium, and a value of 100 and 145 respectively are desired, it is obvious that the replacement of the lacking 25 milliequivalents per liter of sodium chloride will not readily be accomplished by the administration of isotonic (physiologic) sodium chloride solution (145 milliequivalents per liter). So much water would be necessary that extracellular fluids would be decidedly increased. Even 1 liter of isotonic sodium chloride solution per liter of extracellular fluids would increase the concentration of sodium chloride in blood and tissue fluids by only 12.5 milliequivalents; 2 liters of saline solution per liter of extracellular fluids would be necessary to restore the deficit. This amount is obviously impossible to give to any subject whose kidneys are not excreting water. Therefore, the more concentrated the saline solution the more readily will the deficiency be made up. By experiment it was found that intravenous administration of 5 or 6 per cent sodium chloride solution could be tolerated if given slowly, the venous pressure rising only slightly, if at all.

3. Although salt can be given by mouth, the amount usually necessary to restore electrolyte equilibrium may be large (20 to 40 Gm.), can produce gastrointestinal disturbances and may have an erratic rate of absorption. The intravenous route is therefore preferable, although additional amounts may be administered in food or capsules.

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Cases 1 to 8, 11 to 13, 15 and 16 were observed at the Hospital of the Rockefeller Institute for Medical Research, New York. Case 21 was referred by Dr. Gene B. Starkloff. The remainder of the cases were seen on the wards of Barnes Hospital, case 20 from the clinical material of Dr. Edward Massie.

1. Schroeder, H. A.: Studies on Congestive Heart Failure: I. The Importance of Restriction of Salt as Compared to Water, Am. Heart J. **22**: 141, 1941.

2. The term "congestive circulatory failure" is preferred to "congestive heart failure," as the sequence of events leading to "cardiac" edema may be initiated by noncardiac as well as cardiac factors.

3. Any renal or urologic condition causing oliguria or anuria will result in the electrolyte pattern here described unless all the fluids given are balanced by isosmolar sodium and chloride. It is probable, however, that in these conditions the remaining renal function is further depressed by excessive water.

4. Serious consequences resulting from the slow intravenous injection of hypertonic saline solution into a patient already exhibiting a high venous pressure and overhydration are theoretically not to be expected. Injected sodium chloride leaves the blood fairly rapidly, diffusing into extravascular fluids, and probably contributes little to an increase in blood volume except momentarily and until equilibrium between blood and tissue fluids is established.

5. It was found by experiment that diuresis could be initiated when the lacking concentration of salt was restored, cardiac function occasionally improving.

The amount given depended on a calculation of the deficit in plasma, in estimated interstitial fluids and in accumulated edema. Since the kidneys of cardiac patients are deranged but can put out water more readily than salt, reestablishment of their normal balance of sodium chloride was made slowly so as not to "overshoot." Normal extracellular fluid volume was considered as 20 per cent of the body weight. Edema fluid, if present, was roughly estimated from the gain in body weight. Plasma levels of chloride and carbon dioxide–combining power were followed daily; subsequent injections of salt were based on their values. Usually when the plasma level of chloride reached 90 to 95 milliequivalents per liter diuresis was well established. As a rough approximation, for a 70 Kg. man, 17.1 milliequivalents of sodium chloride (1 Gm.) should be expected to elevate plasma levels 1 milliequivalent per liter if edema is not present and salt is not excreted.

TABLE 1.—*Terminal Renal Insufficiency Associated with Overhydration or Electrolyte Loss*

Case	Date	Sex	Age, Yr.	Diagnosis*	Uncontrolled Arrythmia Present †	Duration of Oliguria, Days	Lowest Urinary Volume, Cc.	Lowest Urinary Chlorides as NaCl, Gm.	Chlorides in Plasma, mEq./L.	CO_2, mEq./L.	Response ‡ of Urinary Volume and Cl to Hg.	Av. Daily Fluids Retained (Intake-Output), Cc.	Total Gain in Body Weight, Kg.	Net Loss § of Cl as NaCl in Urine Prior to Oliguria, mEq.	Previous Number of Injections of Hg. and Total Dose, Cc.		Other Contributing Factors and Remarks
1 P. F.	3/29/41	♂	33	R.H.D.	R	5	468	0	76.4 Na 124.5	27.8	0	1,420	1.6	115	2	4	Arrythmia severe Adrenal cortical extract caused diuresis
2 W. D.	9/26/41	♂	42	R.H.D.	S	3	141	0	76.6 Na 111.1	24.5	0	2,120	1.8	...	2	6	Adrenal cortical extract caused diuresis Fluids increased 1,500 to 3,400 cc. per day
3 E. C.	12/30/40	♀	51	R.H.D.	R	6	0	0	76.6‖	....	0	863	2.7	314	4	16	
4 J. K.	12/ 3/39	♀	30	R.H.D.	R	8	70	0	....	....	0	831	3.4	403	3	8	
5 H. M.	9/20/38	♀	45	R.H.D.	R	5	103	0	77.9	....	..	960	1.6	0	0		Fluids increased 1,500 to 3,000 cc. per day
6 O. C.	10/11/39	♂	30	R.H.D.	R	5	65	0	....	....	..	1,280	0	331	2	6	
7 J. S.	10/ 7/39	♂	73	A.H.D.	R	9	48	0	....	....	..	1,122	2.6	190	0		Intravenous 5 per cent dextrose 1,500 cc.
8 H. P.	5/ 5/39	♂	47	R.H.D.	R	2	280	0	....	....	..	1,075	1.5	354	3	7	
9 S. K.	12/10/46	♀	54	H.H.D.	O	5	25	..	69.0 Na 118.4	24.1	..	2,057	2.0	...	0		On rice diet
10 M. J.	11/ 9/48	♂	56	Ca. Biliary fistula	O	5	0	..	87 Na 128	26.4	..	1,350	...	376¶	0		NaCl loss from bile drainage of 1,000 to 2,000 cc. per day

* R.H.D., H.H.D. and A.H.D. denote rheumatic, hypertensive and arteriosclerotic heart disease, respectively.
† Uncontrolled arrythmia indicates that a pulse deficit was present. The arrythmia was always caused by ectopic ventricular beats. R denotes that the apical rate was 90 per minute or more, S that the apical rate was below 90 per minute.
‡ The response of the urinary output of water and chlorides to the intravenous injection of a mercurial diuretic.
§ The total output of urinary chlorides for seven to ten days before the onset of oliguria minus the dietary intake of salt.
‖ Edema fluid.
¶ Estimated.

SUMMARY OF CASES

Of the 21 patients encountered with the low salt syndrome, 10 died and 11 recovered. Most of the former were discovered in retrospect (table 1), and plasma electrolyte values had not been closely followed. Chloride levels were determined in only 4 of the 8 who died of cardiac insufficiency. However, it is probable that the terminal event was renal failure, judging from the rise in nonprotein nitrogen which they all demonstrated, the low urinary volume and the large retention of fluids manifested by the discrepancy between the intake and the output. In 1 instance (case 9) reported elsewhere,[4] the syndrome developed spontaneously while the patient was on the low sodium intake of the rice diet of Kempner [5] with fatal outcome.

In 1 patient (case 3) whose massive edema was being removed by Southey tubes and treated by mercurial diuretics, there was a progressive fall in the chloride content of the fluid from normal levels to 76.6 milliequivalents per liter, as oliguria led to anuria. In the others low plasma chloride levels were discovered after oliguria had occurred.

The development of the "low salt syndrome" is illustrated by the following case.

A woman aged 30 weighed 50 Kg. and was afflicted with subacute and chronic rheumatic endocarditis with involvement of the mitral and tricuspid valves (case 4). Her extracellular accumulation of edema fluid was estimated at about 8 Kg. Her electrocardiogram showed many ectopic beats from various ventricular foci. Her weight varied little during a control period of three weeks. The intravenous injection of 2 cc. of mersalyl and theophylline solution (salyrgan®) caused a urinary excretion of 17 Gm. of chloride calculated as sodium chloride. Three days later the same dose resulted in the excretion of 6.1 Gm. and was followed by progressive diminution of urinary volume, ending finally in oliguria. A later injection of 4 cc. of mersalyl and theophylline solution did not affect urinary water or chlorides. As the patient was ingesting only 1 Gm. of salt per day, the excretion of 23.1 Gm. of salt (395 milliequivalents) accompanied by only 2.2 Kg. of water apparently

4. Schroeder, H. A.; Goldman, M. L., and Futcher, P. H.: The Effects of the Rice Diet upon the Blood Pressure of Hypertensive Individuals, Ann. Int. Med. **30**: 713, 1949.

5. Kempner, W.: Compensation of Renal Metabolic Dysfunction: Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet, North Carolina M. J. **1**: 72, 1945.

depleted her extracellular electrolytes. A week later she had retained 3.4 Kg. of water, which further hydrated and diluted her electrolytes. She died of renal and cardiac insufficiency.

A similar situation resulted apparently from the daily intramuscular injection for twenty days of 2 cc. of meralluride sodium solution (mercuhydrin®).

A man aged 69 with long-standing chronic congestive circulatory failure received daily intramuscular injections of 2 cc. meralluride sodium solution for twenty days (case 14). Except after the first two doses, there was no diuresis; his urinary volume varied usually from 300 to 800 cc. per day but occasionally was as low as 180 cc. He became weak and nauseated, with occasional vomiting; later, considerable drowsiness developed and he complained of cramps in his forearm, calves and thighs. His plasma chlorides were found to be 81 milliequivalents and his carbon dioxide–combining power 32.5 milliequivalents per liter, and there was retention of nitrogen in his blood. He was given 26 Gm. of sodium chloride in 5 per cent solution in two doses without elevating his venous pressure of 260 mm. of saline solution significantly. His plasma chlorides rose to 91 milliequivalents and his carbon dioxide–combining power fell to 27.5 milliequivalents per liter. Moderate diuresis was initiated, after which the nonprotein nitrogen in his blood became lower.

An attempt was made to restore electrolytes to normal by another method in 1 case (chart 1).

A man aged 33 had known rheumatic heart disease involving his mitral valve (case 1). During convalescence from pneumonia, severe right-sided heart failure developed with general anasarca estimated at more than 15 Kg. of fluid. His body weight had declined only 1.5 Kg. in two weeks in spite of two injections of 2 cc. of mercurophylline and the use of a proprietary double salt of calcium theobromine and calcium salicylate. A large discrepancy was noted between his intake of fluids and his urinary volume, although he had lost only 115 milliequivalents of sodium chloride in his urine. It was not surprising, therefore, to find in his plasma a sodium level of 124.5 milliequivalents per liter, a chloride level of 76.4 and carbon dioxide–combining power of 27.8. There was retention of nitrogen in his blood (blood urea nitrogen 27.7 mg. per hundred cubic centimeters). He was given 15 Gm. of sodium chloride intravenously, which initiated a diuresis of water in which chloride values were negligible, caused a loss of 3.5 Kg. in weight and resulted in a moderate elevation of his plasma electrolytes (sodium 129.6, chloride 86.4 milliequivalents per liter). When his weight became relatively stationary adrenal cortical extract (eschatin®) was given daily. No chloride appeared in his urine, but a moderate water diuresis was initiated with a further loss of 4.8 Kg. in weight. His plasma chlorides rose to low normal values (93 milliequivalents per liter) as this occurred, but he died soon after with 144 mg. per hundred cubic centimeters of nonprotein nitrogen in his blood.

Apparently the renal disturbance which he sustained was irreversible, although obvious lesions to account for it were not found at postmortem examination.[6]

In another case, that of a man aged 42 with rheumatic heart disease involving the tricuspid as well as

TABLE 2.—*Renal Insufficiency with Recovery*

Case	Date	Sex	Age, Yr.	Diagnosis*	Uncontrolled Arrythmia Present †	Duration of Oliguria, Days	Lowest Urinary Volume, Cc.	Lowest Urinary Chlorides as NaCl, Gm.	N. P. N.	Chlorides in Plasma, mEq./L.	CO_2, mEq./L.	Av. Daily Fluids Retained (Intake-Output), Cc.	Total Gain in Body Weight, Kg.	Amount NaCl Given I.V., Gm.	Other Treatment	Result, Weight Loss, Kg.	Initiating Factors
11 N. J.	4/ 4/40	♂	67	A.H.D.	R	5	283	0	....	....	....	1,025	2.9	16.0	.....	1.0	Hg. 5 cc. + therapy
12 B. H.	3/12/39	♂	65	A.H.D.	O	5	370	0	....	78.6							
	3/17/39				O	4	639	0	61.0	73.5	....	1,250	2.5	....		0	Hg. 15 cc.
											....	744	3.5	....	Paracent.	3.6	Fluid intake increased 1,000 to 3,000 cc. per day
	5/ 5/39				O	6	321	0	70.4	80.2	....	593	1.6	6.0	Fluid intake lowered	+1.7	Spontaneous
13 J. V.	12/17/40	♀	62	A.H.D.	O	7	30	0	88.6‡	81.6	17.9	1,103	5.3	39.0	Fluid intake lowered	3.9	Hg. 10 cc. + fluid intake increased
14 F. T.	2/22/47	♂	69	A.H.D.	O	8	130	..	56.0	81.0	32.5	859	2.9	26.0	.....	1.5	Hg. 40 cc.; died similar episode
15 A. S.	10/15/38	♂	43	R.H.D.	O	6	400	0	....	....	....	1,443	3.3	....	Fluid intake lowered	0	Hg. 6 cc.; fluid intake increased to 3,000 cc. per day; died similar episode
8 H. P.	4/19/39	♂	47	R.H.D.	R	3	210	0	....	....	....	1,117	2.0	....	Spontaneous recovery	...	Hg. 7 cc.; died similar episode
16 J. P.	9/ 9/39	♂	37	R.H.D.	R	4	450	0	....	....	....	450	1.1	....	Spontaneous recovery	0.4	Hg. 4 cc.
17 A. P.	8/16/48	♂	44	H.H.D.	O	7	0	..	42.0	76.0	35.3	1,756	2.0	63.0	.....	0.9	0.5 Gm. salt diet; no congestive failure
18 B. H.	12/20/48	♀	41	A.H.D.	O	8	200	..	42.0	79.0 Na 116.0	29.5	1,168	2.3	25.0	Blood	...	Hg. 4 cc.; died similar episode later
19 H. B.	10/19/48	♂	30	Chronic glom. nephritis	O	6	200	..	105.0	80.0 Na 123.9	18.2	1,570	4.6	49.0	.....	10.2	Died uremia 3 mo. later
20 B. K.	8/ 6/48	♂	58	H.H.D.	O	5+	300	..	38.0	64.0	54.5	930	...	30.0	Various	...	Hg. 10 cc.; complete recovery—loss of 18 Kg.
21 H. P.	1/19/49	♀	78	Intestinal obstruction	O	4	100	..	64.0‡	75.0	....	2,300	...	21.5	None	...	Excessive injection dextrose in water, loss of 300+ mEq. Cl by gastric suction; recovery rapid

* A.H.D., R.H.D. and H.H.D. signify arteriosclerotic, rheumatic and hypertensive heart disease, respectively.
† Uncontrolled arrythmia indicates that a pulse deficit was present. The arrythmia was always caused by ectopic ventricular beats; R denotes that the apical rate was 90 per minute or more.
‡ Blood urea nitrogen.

6. No characteristic lesions have been noted in the kidneys of the 12 patients coming to autopsy.

other valves (case 2), adrenal cortical extract likewise appeared to initiate diuresis accompanied by a loss of 2.7 Kg. The plasma sodium level, which was initially 111.1 milliequivalents per liter (chloride 77.2), rose only slightly and the patient died. No extra sodium chloride was given, which may have accounted for his failure to recover. A wide discrepancy between the intake and output of fluids was a constant feature of his course.

It would therefore appear that patients depleted of salt may die with low urinary output, retention of water and dilution of electrolytes. During this state nitrogen is retained, weight is gained rapidly and chlorides disappear from the urine. Mercurial diuretics produce little or no response on urinary chlorides or water. Their excessive use may precipitate this condition when the intake of salt is restricted.

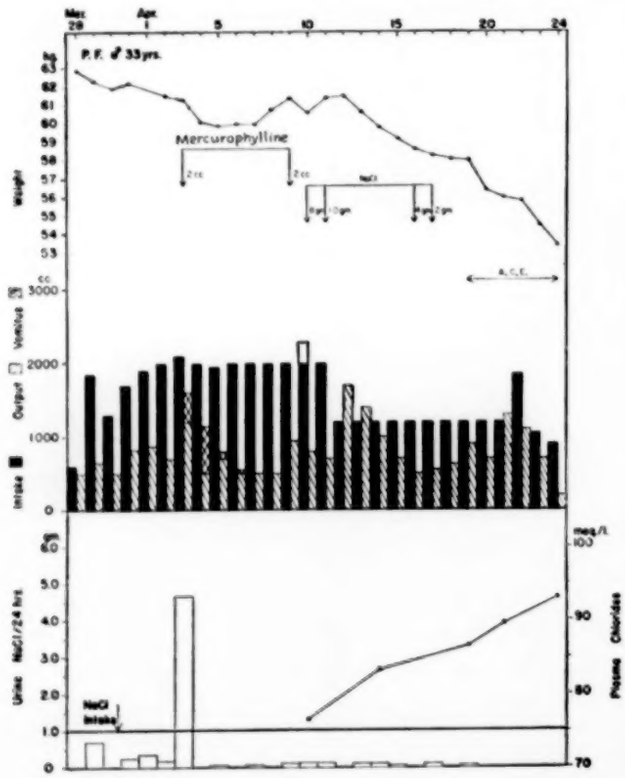

Chart 1 (case 1).—A man aged 33 exhibited congestive failure after an attack of pneumonia. There was considerable discrepancy between his intake and output of fluids, leading to overhydration. In addition he lost 115 milliequivalents of chloride in his urine. On March 10 plasma sodium was 124.5 milliequivalents per liter and carbon dioxide-combining power 27.8. The plasma chloride levels are shown. Blood urea on March 14 was 60.2 mg. per hundred cubic centimeters and his urea-clearance was 30 per cent of normal. Note that both the intravenous injection of 4 per cent sodium chloride solution (shown by arrows) and the injection of adrenal cortical extract (4 to 8 cc. daily, shown by A. C. E.) appeared to initiate diuresis and weight loss, with a rise in the levels of plasma chloride and a retention of chlorides despite the diuresis. On March 19 plasma sodium was 129.6 and on March 21, 131.8 milliequivalents per liter. He died of renal insufficiency.

The reversible features of the low salt syndrome, either from spontaneous remission or therapy with salt, suggest that it is a state of renal insufficiency dependent on low plasma levels of sodium and chloride (table 2). The diuretic and nitrogen-lowering action of hypertonic saline solution has sometimes been dramatic; for example, in the following case.

A man aged 67 (case 11) with arteriosclerotic heart disease and severe ascites and edema lost over 500 milliequivalents of chloride in his urine in ten days as a result of mercurial and xanthine diuretics. His net loss amounted to 329 milliequivalents. The characteristic symptoms and signs appeared, his urinary output diminishing (to a low of 283 cc. on one day). A transfusion of whole blood (500 cc.) did not initiate diuresis, nor did the use of 5 per cent dextrose solution intravenously (1 liter); probably the latter only served further to dilute his electrolytes. But the intravenous injection of 255 milliequivalents of salt (16 Gm.) apparently restored electrolyte balance sufficiently to allow diuresis to begin. Within four days his output increased to well over 1 liter; however, the chloride output of his urine remained exceeding low and his symptoms disappeared. Although he had gained 2.9 Kg. in weight, the diuresis initiated by salt resulted in a loss of this amount and a further loss of 1 Kg.

The mechanisms leading to the development of this bizarre form of renal insufficiency are not known. Some toxic action of mercurial diuretics on the kidneys is probably not the predominating factor; a high fluid intake precipitated the state in 3 instances.

A man aged 65 had ascites and edema resulting from arteriosclerotic heart disease (case 12). He had received three injections of mercurial diuretics at five day intervals, which caused a total loss of 465 and a net loss of 243 milliequivalents of chloride. No mercurial compound was given for fourteen days. When the patient's intake of fluids was raised from 1,200 to 2,500 cc. per day for four days his urinary volume failed to increase; in fact, it became slightly depressed. He became drowsy, disoriented and weak. Chlorides in plasma were found to be 73.5 milliequivalents per liter and nonprotein nitrogen 61 mg. per hundred cubic centimeters. Reduction in the intake of fluids was followed by a diuresis of water, negligible quantities of chlorides appearing in the urine, and his plasma chlorides rose moderately. He continued in a hypochloremic state until relieved by the injection of saline solution and a more liberal dietary intake.

The same case illustrates another point. When the condition is more or less borderline with slight diminution of urinary volume and depression of electrolytes there may be chronic elevation of the nonprotein and urea nitrogen in blood, and the urea clearance becomes depressed. This patient's urea clearance was 46 per cent of normal when his electrolytes were at low normal levels. When his plasma chlorides fell to 73.5 milliequivalents per liter, the urea clearance was 10 per cent of normal and the blood urea nitrogen 67.8 mg. per hundred cubic centimeters. A reversal of the process by the injection of hypertonic saline solution and the addition of salt to his diet resulted in a rise in his plasma chlorides to 93.4 milliequivalents per liter and in his urea clearance to 62 per cent. This phenomenon was observed in other patients. The effect of hypertonic sodium chloride solution in reversing the oliguria is shown in chart 2.

This same type of renal insufficiency may follow excessive loss of chlorides as a result of vomiting when replacement therapy has been inadequate.

A woman aged 78 had had partial intestinal obstruction which was relieved by surgical intervention (case 21). Oliguria and retention of nitrogen in the blood was a constant feature of her postoperative course, and she was believed to be near death. Replacement of the electrolyte loss by hypertonic saline solution resulted overnight in dramatic improvement. Diuresis became established. The blood urea nitrogen fell to normal levels, and the patient was able to resume normal activity. That this change was not coincidental is suggested by the rapid onset of adequate renal function (chart 3).

Of the 11 patients who recovered, either spontaneously or as a result of the injection of sodium chloride solution, 4 subsequently died in a similar state of renal insufficiency. Provided early treatment was instituted, recovery was rapid when salt was given and slow when it was not. Sometimes a dose much less than that

calculated to be ideal began recovery. Excess salt resulted in the accumulation of edema, as is well known.[7]

The injection of hypertonic sodium chloride solution was not accompanied with adverse symptoms when plasma electrolytes were low. Venous pressure was always measured simultaneously; occasionally it fell slightly, more often there was no change, but sometimes it rose 2 to 3 cm. of saline solution after the first 100 cc. had been given, rising no further. The presence of pulmonary congestion did not contraindicate the injection of the hypertonic sodium chloride solution. When the electrolyte concentration in plasma was low, minimum pulmonary edema was observed in 2 cases to regress while sodium chloride solution was being injected. Even large quantities of hypertonic saline solution (6 per cent) sometimes failed to elevate venous pressure significantly above an already high value.[7] Diffusion from blood into tissues was rapid, and higher plasma levels were not always maintained. Plasma chlorides were measured in 2 cases ten to fifteen minutes,

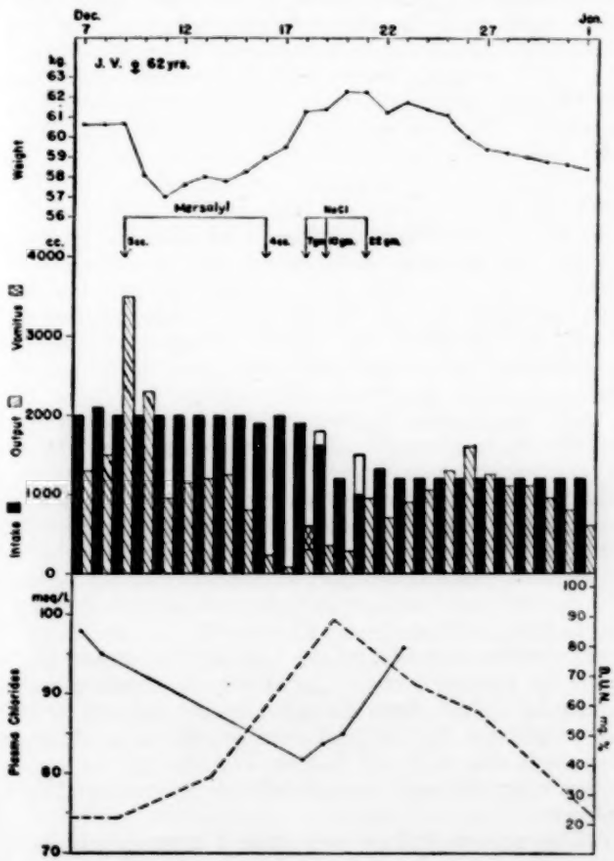

Chart 2 (case 13).—A woman aged 62 displayed chronic congestive failure following the second of two attacks of coronary occlusion. On December 9 the injection of 5 cc. of mersalyl and theophylline resulted in a fall of plasma chlorides. A discrepancy between the intake and output occurred, which was associated with a gain in weight of 5.2 Kg. On December 18 plasma sodium was 124.5 milliequivalents per liter and carbon dioxide-combining power 17.9. On the next day blood urea nitrogen, which had been at normal levels, was 88.3 mg. per hundred cubic centimeters. The injection of 39 Gm. of sodium chloride in 5 per cent solution resulted in diuresis, loss of weight and return of plasma chlorides and blood urea nitrogen to normal levels. Note the lack of response of the urinary volume to mersalyl on December 16. The patient was taking a diet containing 0.5 Gm. of salt daily.

ten to twelve hours and twenty-four hours after the injection. An immediate rise of 7.5 milliequivalents per liter, caused by the injection of 5 Gm. of sodium chloride, produced one of only 3.5 milliequivalents twenty-four hours later. Six grams of salt produced a rise of 7.2 milliequivalents in ten minutes, but only a rise of 2.1 the next day. Both patients were edematous. Their urine did not manifest a significant increase in total chloride content, although the concentration of single specimens was increased.

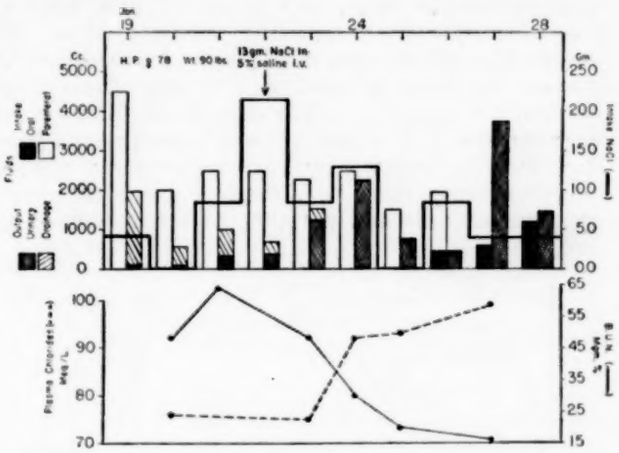

Chart 3 (case 21).—A woman aged 78 had had partial intestinal obstruction, which was corrected surgically. Wangensteen suction drainage from the stomach was instituted postoperatively. There was a large discrepancy between her intake and output of fluids, most of which consisted of 5 per cent dextrose in water injected intravenously. On Jan. 23, 1949 she was comatose and was considered in terminal renal insufficiency. When an attempt was made to correct the electrolyte disturbance by the intravenous injection of 21.5 Gm. of sodium chloride in 5 per cent solution, diuresis became established. Nitrogen retention disappeared, and there was a dramatic improvement in her symptoms with complete recovery.

COMMENT

Peters and Van Slyke [8] have discussed the matter of renal insufficiency resulting from sodium depletion in these words:

> The nonprotein nitrogen of the blood tends to increase in all conditions in which the fluids of the body are greatly depleted, whether the dehydration results from simple deprivation of fluids or from excessive loss of fluid through vomiting or diarrhea. These increases seem to arise chiefly from oliguria, with accelerated protein catabolism and impaired circulation playing contributory roles. A voluminous literature has sprung up about a condition known as "uremia or azotemia from lack of salt," in which it is implied that accumulation of nonprotein nitrogen in the blood is a direct response to depletion of the sodium and chloride of the body. Such a theory finds little physiological support. Deficits of chloride and sodium in the body fluids are generally indications of dehydration. . . . Accumulations of nonprotein nitrogen in the blood in this condition can be eliminated by the administration of enough water to provoke diuresis, although the deficits of chloride and sodium may be aggravated by such therapy. If salt depletion contributes to azotemia at all, it is probably through its injurious effects on bodily functions in general, and especially upon the circulation, not because it has any particularly deleterious influence upon the kidneys. It has been reported [9] that injections of small volumes of concentrated sodium chloride solution are beneficial in restoring the excretory activity of the kidneys; but such salt injections increase the volume of extracellular fluid by abstracting water from the tissue cells, thereby providing more water for the formation of urine.

They have suggested further that the elevation of blood urea is "probably only a manifestation of the circulatory collapse which results from sodium depletion," disagreeing with certain European writers on the subject.[9]

7. Futcher, P. H., and Schroeder, H. A.: Studies on Congestive Heart Failure: II. Impaired Renal Excretion of Sodium Chloride, Am. J. M. Sc. **204**: 52, 1942.

8. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, ed. 2, Baltimore, Williams & Wilkins Company, 1946, vol. 1, p. 663.

9. Chabanier, H., and Lobo-Onell, C.: Hypochlorémie et accidents post-opératoires, Paris, Masson & Cie, 1934.

The syndrome here described appears to be a state of renal insufficiency dependent on a disturbance of the normal concentration of sodium chloride in extracellular fluids. It is not dehydration, as absolutely defined, because large stores of water containing dilute sodium chloride solution may be present. It is not dependent on alkalosis, for the carbon dioxide–combining power of the blood may be altered only slightly. It can be initiated by depleting the body of sodium chloride through the use of either mercurial diuretics or other measures, by producing a large discrepancy between the intake and the output of fluid or by excessive loss of salt through abnormal routes. It is often reversible by restoring the concentration of sodium chloride in body fluids to normal, a procedure which can cause diuresis and a return of renal function to higher values. It may accompany but is not always dependent on circulatory insufficiency; it is usually associated with prior renal disturbance, either functional or organic.

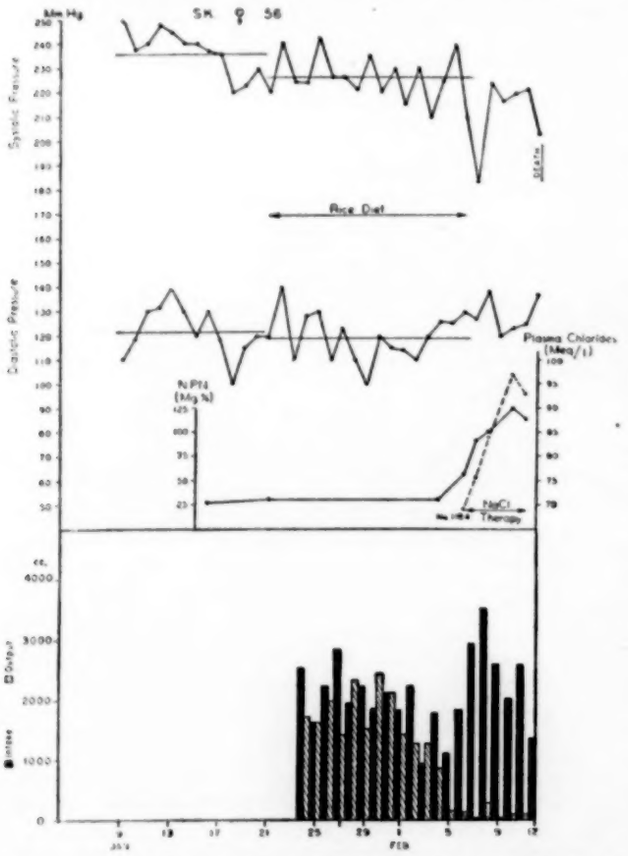

Chart 4 (case 9).—A woman aged 56 had rapidly progressive hypertensive vascular disease without retention of nitrogen but with diminution of renal function. When she was given a diet containing 0.5 Gm. of salt (rice diet) oliguria developed fourteen days later. This development was rapid, and the patient complained of nervousness, apathy, loss of appetite and weakness. Her intake of fluids remained high in spite of the obvious overhydration which was developing. Plasma chlorides were low, as was sodium, and an attempt to reverse the oliguria by the use of intravenous hypertonic saline solution was to no avail. She died of uremia.

It is probable that the excessive use of dextrose solution in water without sodium chloride postoperatively contributes to renal insufficiency and initiates the low salt syndrome in elderly patients or in those who already have some renal disturbance of minor degree. The recognition of this syndrome becomes important, because immediate therapy may be life saving. Delay has resulted apparently in irreversible changes in the function of the kidneys.

This condition is apparently the same as one described recently by MacGuire,[10] who reported 3 cases of hypertension associated with congestive failure. On diets low in salt, and in 2 instances after the use of mercurial diuretics, blood urea levels rose considerably only to fall when salt was added to the diet. Electrolyte levels in plasma were not reported, however. A related situation may be one reported by Muirhead and Fromm,[11] who found dilution of extracellular sodium and chloride in the syndrome of acute renal insufficiency. It is possible that many cases of so-called postoperative, reflex or essential anuria belong in the group here discussed. Renal failure resulting from the "salt-losing nephritis" of Thorn, Koepf and Clinton [12] may depend on the same underlying mechanism, although the kidneys of their patients were able to excrete large volumes of water. Chabanier and Lobo-Onell [9] have described at length a condition occurring after operations, characterized by hypochloremia and azotemia with low urinary output reversed by the intravenous administration of hypertonic saline solution. Although blood pressure was often lower when this state had developed, shock was not present. Recently, Soloff and Zatuchni [13] reported 7 cases (4 fatal) of this syndrome in congestive failure and in hypertension treated by isotonic sodium chloride solution. They stated that it is not uncommon. They did not stress, however, the oliguria which in my experience accompanies this condition (chart 4). These observations indicate that there may sometimes be an inverse ratio between sodium and chloride in body fluids and nitrogenous products in the blood; they further suggest some obscure relation between the concentration of sodium chloride in plasma and the ability of the kidneys to excrete nitrogen. It must be emphasized that serious disturbances of acid-base balance were not present.

The mechanism whereby lowered electrolytes contribute to renal insufficiency is unknown. The lowered urea clearance and elevation of the blood urea suggest that renal blood flow is reduced. More exact studies will be necessary to prove this point. Theoretically, if adequate water is available and plasma is being filtered by glomeruli, normal kidneys should be able to excrete water and retain salt until electrolyte balance is restored. That these kidneys can excrete water to some extent is shown by the two experiments in which adrenal cortical extract apparently initiated a water diuresis. That these kidneys cannot excrete salt is demonstrated by the negligible quantities of chlorides in the urine and the failure of chlorides to appear even when diuresis was stimulated by mercurial compounds.

The normal kidney performs a marvelously exact function of regulating body fluids and electrolytes and maintaining acid-base equilibrium. The abnormal (hypertensive, cardiac or aged) kidney may be deficient in some of these functions. Whether the low salt syndrome occurs only in the presence of renal disease or renal functional disturbance and never develops when the kidneys are perfectly normal cannot be stated at this time. In every patient observed the kidneys were diseased functionally from congestive failure or anatomically from other causes.

10. MacGuire, W. B., Jr.: Risk of Uremia Due to Sodium Depletion, J. A. M. A. **137:** 1377 (Aug. 14) 1948.
11. Muirhead, E. E., and Fromm, C. S.: Severe Acute Renal Insufficiency with Recovery, J. A. M. A. **137:** 1378 (Aug. 14) 1948.
12. Thorn, G. W.; Koepf, G. F., and Clinton, M., Jr.: Renal Failure Simulating Adrenocortical Insufficiency, New England J. Med. **231:** 70, 1944.
13. Soloff, L. A., and Zatuchni, J.: Syndrome of Salt Depletion, J. A. M. A. **139:** 1136 (April 23) 1949.

Congestive circulatory failure is the result of a renal disturbance of salt-and-water-regulating mechanisms. The syndrome here reported represents in some respect the advanced stage of that disturbance in which neither salt nor water is excreted. The deficiencies of the cardiac, diseased or aged kidney, therefore, may contribute to a precarious state of water and salt balance which can be disturbed by well meant therapeutic measures into fatal deficiencies of other functions.

The mechanism of the partial renal shutdown is not understood, but the sequence of events may be somewhat as follows:

1. Salt depletion from mercurial diuretics,[14] excessive hydration due to a high intake of fluids or, perhaps, spontaneous failure of the kidneys to excrete water occurs.
2. Some stimulus resulting from an abnormally low sodium chloride level in plasma or extracellular fluids causes a reduction in renal blood flow or an excessive tubular reabsorption of both salt and water. Water moves into cells, disturbing their function.
3. Urinary volume is diminished and nitrogen retention begins.
4. Continued intake of fluids enhances the relative overhydration. The function of myocardial as well as other cells is altered adversely by this dilution of *le milieu intérieur*.
5. Uremia from renal shutdown develops.
6. When the proper balance of sodium chloride in fluids is restored *le milieu intérieur* becomes more favorable for cellular function and the kidneys again begin to excrete water and nitrogen.

The return of renal function probably is not dependent on a restoration of circulatory efficiency through increases in the blood volume, for venous pressure, a rough indication at least of the state of the blood volume, was not reduced during anuria. Nor is it dependent on adequate levels of blood pressure. Although in some cases the blood pressure tended to be lower, in others there was little change and in the 2 patients with severe hypertension blood pressure remained high. It is probably not dependent on the abstraction of water from cells to make water available for the kidneys; plenty of water was often available. Cellular hydration in the kidneys, as elsewhere, may have interfered with function, adequate concentrations of sodium chloride removing water from cells and in some manner increasing renal and cardiac function.

The use of hypertonic sodium chloride solution for making up the salt deficit deserves comment. The use of solutions composed of concentrations of sodium chloride necessary to overcome deficits is much more logical than is the routine employment of isotonic sodium chloride solution. When overhydration is present and relative acid-base balance is undisturbed, sodium chloride in concentrated solution should be used (Gamble,[15] his chart 35 C). Concentrations as great as 20 per cent have been advocated.[9] When dehydration is present and there is a water deficit, water should be used. Only when deficits of both are present to an equal degree is isotonic sodium chloride solution the concentration of choice. When acidosis or alkalosis are found, the fluid which is administered should contain anions or cations to make up the deficit. Good kidneys can compensate for errors in the concentrations of electrolytes administered; poor kidneys, or those with disturbed function, often cannot. The intelligent use of fluids therefore requires a knowledge of the relative concentrations of electrolytes in plasma and a readjustment of those in the fluids administered to compensate for deficits. The use of standard concentrations for all purposes is to be deplored.

The hazards of the rigid restriction of sodium chloride in the diets of cardiac patients, used concomitantly with mercurial diuretics, cannot be overemphasized. The low salt diet has proved a valuable adjunct to the management of congestive circulatory failure, preventing the accumulation of edema fluid. However, when agents which act specifically to increase the renal excretion of chlorides are also used, depletion of salt can be expected. Theoretically, the same situation might occur if the sodium in intestinal fluids were bound by adsorption on to the newer ion-exchange resins.[16] If deficits of salt can be produced in the body by these resins the frequent occurrence of this syndrome can be predicted from their use. It therefore becomes obvious that careful attention must be paid to the water and electrolyte balances of the body when these disturbances of balances are being treated, and especially when the intake of sodium chloride is severely restricted.

SUMMARY AND CONCLUSIONS

A syndrome of renal failure has been described which results from (*a*) retention of water and dilution of electrolytes or (*b*) excessive depletion of body salt, usually by the use of mercurial diuretics. Sometimes this condition can be reversed by the intravenous injection of hypertonic sodium chloride solution in amounts sufficient to restore electrolyte-water equilibrium. This syndrome is not uncommonly seen in congestive circulatory failure.

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ABSTRACT OF DISCUSSION

DR. J. EDWIN WOOD JR., Charlottesville, Va.: The syndrome which Dr. Schroeder describes has been encountered by many physicians. Fortunately, in patients treated outside the hospital, an extremely low salt diet is difficult to maintain. Twenty-four hour urinary sodium excretion tests indicate clearly that many patients actually have a higher intake of sodium than that prescribed. My associates and I have used mercury sparingly outside the hospital, and consequently our cases of low salt syndrome have occurred in patients in the hospital with severe heart failure or in hypertensive patients purposely thrown into this state with a low sodium diet and repeated mercurial injection. In this latter group, the blood pressure invariably falls in our experience and the azotemia seems to be related to this, with an accompanying diminution in glomerular filtration rate. The picture Dr. Schroeder describes in treated congestive circulatory failure of long standing certainly may have added contributory factors, but the basic mechanism of diminished renal blood flow may also be present. It is interesting to speculate that the low serum level of sodium or chloride, or both, may adversely affect renal function in some way, but just how and whether this is really true remains to be seen. McCance in 1936 produced a similar low salt syndrome in normal subjects with similar symptoms: accompanying azotemia and low serum sodium and chloride values following salt restriction and induced sweating. McCance was of the opinion, after appropriate studies, that diminished glomerular filtration was a prime factor. Of course, the subjects did not have edema but were allowed large amounts of water so that the extracellular features were essentially the same. Therefore, a damaged kidney or one with chronic circulatory disturbance does not appear to be prerequisite for the production of the syndrome. In this regard, a better understanding of potassium excretion would help. Possibly, long periods of dietary sodium depletion have led to potassium

14. Schroeder, H. A.: Studies on Congestive Heart Failure: IV. The Effect of Various Diuretics on the Excretion of Water and Chlorides, to be published.
15. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluids, Cambridge, Mass., Harvard University Press, 1947.
16. Dock, W.: Sodium Depletion as a Therapeutic Procedure: The Value of Ion-Exchange Resins in Withdrawing Sodium from the Body, Tr. A. Am. Physicians **59**: 282, 1946.

depletion as well, and although one would expect potassium retention during the low salt syndrome, actually a total deficit might be present. It is possible that replacement of potassium as well as sodium should be considered in some cases. Incidentally, in the intermittent use of ammonium chloride large amounts of urinary potassium may be lost, particularly in the first three or four days of ammonium chloride dosage. Whatever the mechanism involved in the production of the low salt syndrome, we should be constantly aware of the possibility and seek a better understanding of the reason for recovery in some patients but not others, following administration of hypertonic saline solution. The too frequent use of mercurial diuretics may lead to undesirable states. Absence of diuresis following use of a mercury compound is most important and at once raises a suspicion that low salt syndrome may be present. If this is determined by a study of the electrolytic pattern, emphasis should again be placed on the point that the patient has "water intoxication," and remedial salt must be given in hypertonic solution, as pointed out by Dr. Schroeder.

DR. HENRY A. SCHROEDER, St. Louis: It seems to me that the pendulum has swung too far on the question of salt restriction. If one takes a general philosophic point of view on any new therapeutic procedure and new methods for intensifying it, one may expect to find symptoms and disturbances dependent on this form of therapy. As Dr. Wood said, the low salt syndrome probably has not been seen more frequently because diets have not been low enough. With the development of salt-free milk, one can maintain an adequate protein intake with a lower intake of sodium chloride. The use of the new ion-exchange resins, which appear to absorb sodium from the gastrointestinal tract, may lead to more cases of this condition if the intake of sodium chloride is severely restricted as well. The use of a mercurial diuretic every day as a maintenance dose has in my experience and in that of others led to the development of the low salt syndrome. I agree with Dr. Wood that shock or a state of semishock may contribute somewhat to the low renal blood flow and diminished excretion of sodium chloride, but in many cases there is no clinical evidence of shock, at least during the onset of the condition. The question of potassium loss is important and deserves further study. It should be pointed out that mercurial diuretics may increase the excretion of potassium and even of calcium and magnesium under certain conditions. There is also a chronic state of this condition in which there is diminution of renal function for weeks, with oliguria and nitrogen retention which may reverse itself on administration of adequate electrolytes and restoration of their concentrations.

Paraplegic Patients.—It is unfortunate that many paraplegic patients misunderstood the assurances given them by the Army that over 80 per cent of them would walk. These tragic individuals have learned in these last few years the difference between ambulating and walking. They, quite naturally, had expected to walk in the manner to which they were accustomed before their injury and irrespective of the level of that injury. This overenthusiastic approach did more harm than good and led to ill advised actions by members of Congress and other well meaning laymen which made the paraplegic patient consider himself in a group set aside from other seriously wounded and permanently handicapped veterans. The problems of the care and treatment of patients with paraplegia must be thoughtfully carried out to a solution. There is no doubt but that the problems of these patients have been built up too strongly in the public mind. They have become the center of much interest, not all medical, which may eventually make their care even more difficult. The very word "paraplegic" is objectionable. It is frequently heard from the lips of patients and lay persons, singling out and stamping these patients as doomed with a special and completely hopeless disability. A less pointed, less specific term should be adopted. These patients are seriously and tragically injured persons and should be treated as such, but they should not be singled out for overindulgent publicity from those with other types of injury just as serious and, in many cases, more disabling.—Loyal Davis, M.D., *Surgery, Gynecology and Obstetrics*, July 1949.

THE GENERAL MANAGEMENT OF RHEUMATOID ARTHRITIS

CHARLES RAGAN, M.D.
New York

What is described as rheumatoid arthritis may represent more than one disease. The onset is variable, the course is characterized by remissions and exacerbations, and it is impossible to forecast the future course of events in the individual patient. Diagnosis is difficult in early cases, and an exact prognosis may be difficult even in cases of long duration.

This paper will concern itself solely with rheumatoid arthritis of the peripheral joints. Rheumatoid, or Marie-Strümpell, spondylitis will not be discussed, because it is apparently a different disease and in our opinion should not be classified as rheumatoid arthritis. The reasons for this exclusion are several. The sex distribution is entirely different. In rheumatoid spondylitis 80 per cent of the patients are men, but in rheumatoid arthritis only 23 per cent are men. The agglutination of group A hemolytic streptococci is positive in 50 per cent of patients with rheumatoid arthritis,

Distribution of Peripheral Joint Involvement

	Rheumatoid Arthritis of Spine (Marie-Strümpell) 169		Typical Rheumatoid Arthritis (Peripheral Joints) 85	
Number of Patients	Number	Per Cent	Number	Per Cent
Spine only	63	37	0	0
Hip	42	25	13	15.3
Shoulder	36	21	45	53.0
Knee	45	27	63	74.3
Ankle	19	11	54	63.5
Foot	17	10	40	47.0
Elbow	7	4	40	47.0
Wrist	6	4	60	70.6
Hand	16	9	79	93.0
Jaw	2	1	4	4.7

but such tests have been positive in only 2 per cent of 169 cases of spondylitis. In this 2 per cent there was no peripheral joint involvement associated with the spondylitis. Subcutaneous nodules are present in 10 to 20 per cent of patients with rheumatoid arthritis, but, according to Simpson and Stevenson,[1] are absent in rheumatoid spondylitis. In the 169 cases of this series the distribution of peripheral joint involvement differed greatly from that seen in 85 cases of typical rheumatoid arthritis (see the table).

USUAL OUTCOME OF RHEUMATOID ARTHRITIS

Treatment is directed toward changing the natural course of a disease. Hence, before the treatment of rheumatoid arthritis is discussed, it is important to have some information on its natural history. If patients with rheumatoid arthritis are followed over a long period of time, their ultimate physical state will fall into one of the following five categories: (1) bedridden

Aided in part by a grant from the Masonic Foundation for Medical Research and Human Welfare.

From the Edward Daniels Faulkner Arthritis Clinic of the Presbyterian Hospital and the Department of Medicine, College of Physicians and Surgeons, Columbia University.

Read before the Joint Meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. Simpson, N. R. W., and Stevenson, C. J.: An Analysis of Two Hundred Cases of Ankylosing Spondylitis, Brit. M. J. 1: 214, 1949.

or chair-ridden; (2) deformities or flexion contractures with continuing complaints of joint pains (i. e., disease still active and may be progressing); (3) deformities or flexion contractures without complaints (commonly called burnt out cases); (4) occasional joint pains without deformities or flexion contractures which interfere with existence, and (5) no signs of arthritis.

It has been possible to follow 374 patients with rheumatoid arthritis for more than five years. The mean period of observation was eleven years, the longest follow-up period has been twenty years. These patients were seen in the Edward Daniels Faulkner Arthritis Clinic of the Presbyterian Hospital. The diagnosis was made by at least three clinicians. The average duration of arthritis before the first visit was between one and two years. At the end of the period of observation, it was possible to classify each patient according to one of the categories previously mentioned. Ten per cent were confined to bed or chair; 28 per cent had flexion contractures and the arthritis was active; 12 per cent had flexion contractures with inactive arthritis. A considerable number (26 per cent) at the termination of the period of follow-up had no evidence of arthritis, and another large group (22 per cent) had minimal complaints (occasional joint pains) referable to their arthritis. The patients who had a good end result achieved this with varying forms of therapy and in some instances with little or no treatment. In these patients the institution of heroic but potentially dangerous therapeutic measures would not have been justified. However, in the group of patients who were bedridden or had deformities and flexion contractures which interfered with their economic and social existence (39 per cent) the situation is different. A therapeutic measure which might have dangerous potentialities or which might interfere with the patient's life situation would be justified if the ultimate outcome was improved. Among potentially harmful therapeutic agents are the following: (1) gold compounds—which will be discussed in another paper; (2) multiple transfusions; (3) radiotherapy, and (4) fever therapy. Forms of treatment which seriously interfere with a patient's life situation are (1) rest, including bed rest and (2) climatotherapy.

PROGNOSIS

Before the institution of therapy in a disease with such a variable outcome, every attempt should be made to differentiate the patient with a good prognosis from the one who will do poorly. Short and Bauer [2] in their study eliminated many factors which in their opinion had no prognostic value. These included the following: sex, prodromal symptoms, progressive or intermittent course before admission, acute or gradual onset, presence of anemia, family history of rheumatoid arthritis or rheumatic fever, and onset in relation to the menopause. Patients seen in the first year of their disease did better than the group as a whole, and patients with severe symmetric involvement—typical rheumatoid arthritis—did less well than those with atypical forms of the disease. It is believed that in the absence of serologic or roentgenographic evidence of rheumatoid arthritis, the diagnosis of the disease in the first year is extremely difficult and the possibility of a mistaken diagnosis is great. In the patients we have followed, an attempt was made to exclude adult rheumatic fever simulating rheumatoid arthritis by use of serologic tests in addition to the usual clinical and roentgenologic methods. Forty patients were observed during approximately the same period who had adult rheumatic fever clinically indistinguishable from early rheumatoid arthritis, and these patients recovered completely from their arthritis. In the group of 374 patients with rheumatoid arthritis, 104 were seen in the first year of their disease. Of the 104, 16 per cent had arthritis for less than one year and had no recurrence. The patients in this 16 per cent originally were thought to have rheumatoid arthritis. In retrospect, that diagnosis may have been in error. Therefore, in the absence of a severe typical disease, prognosis is almost impossible on clinical grounds. It has been our impression for many years that a positive test for agglutination of group A hemolytic streptococci in the serum of a patient with rheumatoid arthritis was of poor prognostic significance, and in this group of patients this impression seems to be borne out. Forty-six per cent of the patients had a positive streptococcus agglutination and 46 per cent a negative (results were doubtful in 8 per cent); therefore these groups are comparable. The first 3 categories—bedridden, flexion contractures but active, and flexion contractures and inactive—may be considered a poor end result, while occasional joint pains and no arthritis is a good end result. In the group with a positive agglutination (fig. 1) 70 per cent had a poor end result, while in the group with a negative agglutination 68 per cent had a good end result. Thus a positive streptococcus agglutination test is a poor prognostic sign. This correlation is far from

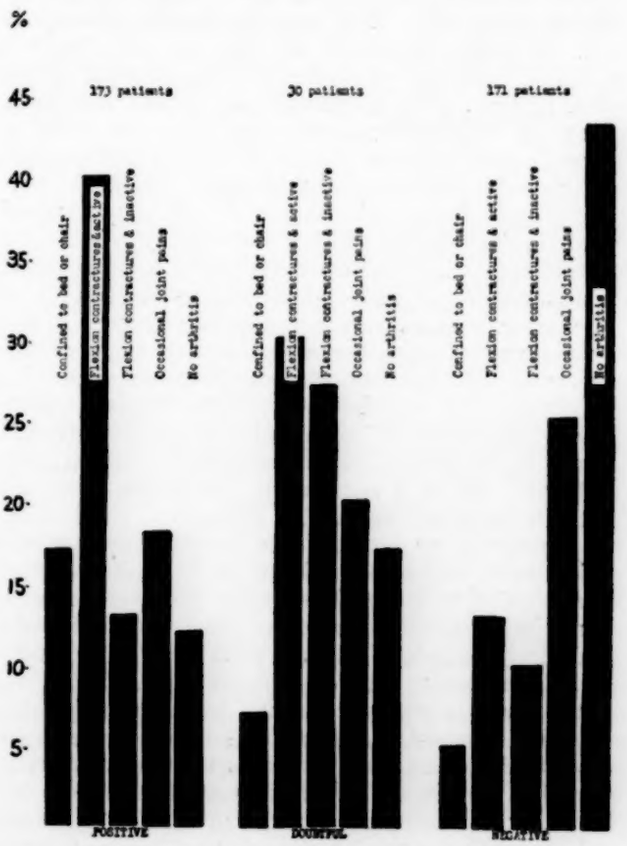

Fig. 1.—Physical state of patients with rheumatoid arthritis at the end of period of observation according to their original group A hemolytic streptococcus agglutination. (Percentages are of the total of each group; 172 positive, 171 negative.)

2. Short, C. L., and Bauer, W.: The Course of Rheumatoid Arthritis in Patients Receiving Simple Medical and Orthopedic Measures, New England J. Med. **238**: 142, 1948.

absolute, for some patients with a positive agglutination do well and some with a negative agglutination end badly. However, it is now believed that the presence of severe typical rheumatoid arthritis or a positive streptococcus agglutination warrants heroic measures.

VALUE OF VARIOUS FORMS OF THERAPY

The value of various forms of therapy in rheumatoid arthritis must be considered in the light of the foregoing discussion of its natural history.

Rest and Exercise.—As has been stated, chrysotherapy will not be discussed herein but attention will be confined to certain measures which are directed toward improvement of the general health of the patient. The value of these measures has not been proved by statistical studies, but it is generally considered to be real. The most important measure is rest. By rest is meant rest for the body as a whole—in bed, if necessary—and rest for the inflamed joints, either by bed rest or by splinting in plaster. Rest must always be supervised; when unsupervised, bed rest is worse than no rest at all. The ideal is rest coupled with exercise. Exercise should always be within pain and fatigue limits. It should be directed toward strengthening muscles which if lost will result in flexion contractures, which are to be avoided if at all possible. Rest should be graduated, depending on the activity of the disease. It may vary between complete rest in bed for the patient with the severe, active stage of the disease to brief periods on a couch before dinner for the patient with a mild form of the disease. Some believe that ideally the patient with rheumatoid arthritis should be treated as is the tuberculous patient with prolonged care in a sanatorium. However, there are certain obvious defects in this argument. First, there are practically no facilities for hospitalization of the patient with rheumatoid arthritis in the United States; economically, it is not feasible for the average wage earner or housewife to have this. Second, there is some doubt in the minds of patients with rheumatoid arthritis that prolonged bed rest benefits them. Some feel that stiffness is intensified by it. In the Scandanavian countries, where hospital facilities for prolonged care are available, the search continues for a specific treatment for the disease. In a limited experience in the arthritis clinic, using the facilities of Goldwater Memorial Hospital, the results of prolonged bed rest, exercises and a nutritious diet were not impressive, even though rest is generally considered to be of great importance.

Prevention of Deformities.—The prevention of deformites is also in this same category. Flexion contractures should be prevented if possible by the use of molded plaster splints. These can be worn with practice and encouragement by the average patient but should be removed at regular intervals for supervised exercise. Since we have followed patients who have continued to have an active form of the disease for over twenty years, this continued supervision may be difficult. However, in the acute episode such simple plaster splints can be exceedingly helpful. The detailed treatment of flexion contractures is the subject of another paper.

Salicylate and Other Therapy.—The drug of choice in the treatment of rheumatoid arthritis is salicylate. Obviously opiates are to be avoided in such a chronic disease, but small doses of codeine may be used to tide a patient over a crisis. Use of aminopyrine is to be avoided. In 3 documented cases agranulocytosis has occurred in patients with rheumatoid arthritis who had been given this drug. Cinchophen and neocinchophen are also to be avoided because of their potentialities as hepatic poisons. Salicylate is a relatively innocuous drug, and the patient with long-standing rheumatoid arthritis has confidence in it. Time and time again patients have stated that acetylsalicylic acid is the only drug which has helped them. At the clinic we have not been able to convince ourselves that there is any difference between sodium salicylate and acetylsalicylic acid as to effectiveness or toxicity. Enteric coating of either may permit an increased dosage to be tolerated. Sodium bicarbonate should be avoided, since the salicylate blood level falls and free salicylate excretion in the urine increases following its administration. Aluminum hydroxide preparations relieve some of the gastric distress, do not interfere with salicylate metabolism and can be given with salicylate. Para-aminobenzoic acid has recently been advocated as an adjunct to salicylate therapy to increase the blood level and to decrease the excretion of free salicylate. The work is based on priming doses of para-aminobenzoic acid. In our experience, this drug causes a certain amount of gastric irritation, and the use of 8 Gm. of it in conjunction with 3.6 Gm. of sodium salicylate failed to raise the blood level and did not materially influence the excretion of any of the salicylate fractions studied in the urine including salicyluric acid, free salicylate, salicyl-glucuronide and gentisic acid. This approaches the maximum dose of para-aminobenzoic acid which our patients are able to tolerate or take conveniently in conjunction with salicylate. We have found that it is simpler to increase the amount of salicylate administered. Salicylate acts as an analgesic to the best of our knowledge in rheumatoid arthritis, and this analgesic effect is not complete. Flexion contractures may develop on full salicylate dosage.

Physical Therapy.—Physical therapy is important, and simple measures which the patient can perform by himself at home are the most effective. Muscle-setting exercises within pain and fatigue limits should be encouraged strongly. Active exercise for the patient able to perform it and passive exercises when active exercises cannot be carried out are the mainstays of the physical treatment for these patients. Again, the aim is to prevent flexion contractures by rebuilding extensor muscle groups and thereby overcoming the stronger flexor groups.

The place of psychotherapy has not as yet been fully evaluated. In the prodromal period these patients may often experience emotional shocks. Intensive psychotherapy is a tedious process. Often when the psychiatrists have been asked for help, lack of insight or an immature attitude on the part of the patient has prevented help from such therapy. Patients with severe long-standing rheumatoid arthritis are chronically ill, with all that term implies of a warped and dismal outlook on life in general. Whether this is the result of the disease or the cause of the disease one cannot say.

Effect of Climate.—Adequate studies have not been carried out concerning the effect of climate on patients with rheumatoid arthritis. In Sweden [3] a tropical ward

3. Edström, G.; Lundin, G., and Wramner, T.: Investigations into the Effect of Hot, Dry Microclimate on Peripheral Circulation, etc., in Arthritic Patients, Ann. Rheumat. Dis. 7:76, 1948.

has been used, and a majority of the 18 patients studied have shown objective improvement after a stay of one hundred days in this ward. In a disease with such a variable prognosis a large series of patients would have to be studied to arrive at a definite conclusion. Against the indefinite benefit to be derived from a move to a more equable climate must be weighed the economic hardships as well as the disruption of family ties. Our policy has been to suggest this only if financial hardships will not develop and if serious dislocation of family relationships will not follow such a move.

Blood Transfusions.—Multiple transfusions have been advocated for the patient with rheumatoid arthritis. In some cases a temporary response may follow such a series, but no studies have been reported which would be acceptable in the light of the varied end result described here. After many and frequent transfusions the hazards of homologous serum jaundice are real, and in a disease with such a chronic course many transfusions would be necessary. Barsi's report on the curative effects of transfusions of blood from pregnant women has not been confirmed in this country, but recently the use of pooled postpartum plasma has been favorably reported. Various fractions of blood—red cells, serum albumin and gamma globulin—have not in our experience been followed by dramatic improvement. Lyophilized plasma has had such grave potentialities as a harborer of homologous serum jaundice that, after a fatality occurred, we have hesitated to use it and have had no experience with irradiated lyophilized plasma.

Radiotherapy.—The results of radiotherapy in rheumatoid arthritis have been disappointing. This is in direct contradistinction to its effects in Marie-Stümpell spondylitis, for which many believe that radiotherapy is the treatment of choice. Isolated reports have described the beneficial effects of radiotherapy on single peripheral joints, but in our experience the results have been extremely variable and do not warrant exposure of the patient to a possibly harmful agent.

Fever Therapy.—Fever therapy—induced either by external heat or by reaction to a foreign protein—has been used widely and in the experience of some it offers temporary relief. Others believe that the rigors to a sick person are too violent and that the benefit which is obtained is too brief to justify use of fever therapy.

Rehabilitation for living is an extremely important phase of the treatment of the patient with rheumatoid arthritis. This includes an emotional acceptance of deformities, with physical correction of such as it is possible to alter. It also includes economic rehabilitation whereby a crippled person may be taught a trade by which he may become free, at least in part, of the charity of relatives or of the state. This is possible with a great number of patients, but a willingness to withstand pain to gain a degree of activity is essential, and some patients never achieve this goal.

SUMMARY AND CONCLUSION

The aim of the physician in the treatment of the patient with rheumatoid arthritis should be to allay pain and to prevent flexion contractures or deformities as far as is possible. Although pain may not be completely relieved, if the patient can be encouraged to keep an optimistic attitude—and the end result described here is not too discouraging—his prognosis should be favorable. Once deformities have ensued, a program of reeducation for economic and social self sufficiency is extremely important.

Previous to the announcement by P. S. Hench and associates [4] of the use of compound E of Kendall in the treatment of rheumatoid arthritis, little more than these simple measures could be advocated to change the final outcome of this disease. It is to be hoped that further study of this therapeutic agent may lead to a better understanding of rheumatoid arthritis and to a far different end result after the patients treated with compound E have been followed for five years.

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ABSTRACT OF DISCUSSION

DR. HANS WAINE, Boston: Having described rheumatoid arthritis as a generalized disease of unknown cause, Dr. Ragan correctly stipulates treatment for the total patient, not only for his joints or his foci of infection or his sedimentation rate. He has given the outline of a broad program, one which is based on empirically useful principles and one in which I would follow him in every point. Due emphasis has also been laid on the wisdom of preventing deformities, so as to curtail the tedious and expensive job of rehabilitation later on. It is true that scarring and damage to articular tissues will inevitably result if the inflammatory process persists for longer than a few weeks. Fortunately, socially and economically significant loss of function need not occur. It should be remembered that functional impairment need not be proportionate to either severity or chronicity of synovitis, provided proper precautions are used to insure continued motility by controlled exercises and by the reduction of crippling spasm. In my experience, this disease spontaneously becomes inactive or nearly so in about 30 per cent of patients observed for an average of three years. It therefore follows that at least in this group of patients the maintenance of a high degree of functional capacity is of great importance. As these preventive measures make the most strenuous demands on time and ingenuity of physicians and severely tax the resources of hospitals and patients, one would welcome a reliable prognostic guide during the early stage of disease to allow one to separate the group of patients who have a favorable prognosis. In this respect, the report of correlation between initial serum agglutinations to group A hemolytic streptococci and the continued activity of rheumatoid arthritis is most interesting. I should like to inquire how many tests were necessary in the individual case and within what time after the start of observation the information could be gathered, whether the titers appeared significant and how the results compared to information given by the sedimentation rate. My associates and I have not in our series checked the prognostic value of agglutination reaction, but it is to be hoped that further analyses may substantiate Dr. Ragan's claim for an objective index. Given this information, then, the physician might have one further tool, aside from the general clinical impression, for predicting the outcome of the disease in patients with severe rheumatoid arthritis.

DR. CHARLES RAGAN, New York: The agglutination of group A hemolytic streptococci has been found to be positive in the first year in about 35 per cent of the patients. After the first year, it runs consistently between 50 and 55 per cent positive. The titer has no great significance. The agglutination should be called positive when there is strong agglutination in the lowest titer. If the titer runs high with weak agglutination in the lowest titer, it is not considered a positive reaction. There is some correlation with the sedimentation rate, but this is not absolute. We have seen patients with a normal sedimentation rate and a positive streptococcus agglutination with poor outcome and some with a greatly elevated sedimentation rate and a negative agglutination who do well. In regard to the types of rheumatoid arthritis, no difference has been observed between atypical and typical rheumatoid arthritis as far as the end result is concerned; usually the streptococcus agglutination is positive in typical severe rheumatoid arthritis.

4. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: The Effect of a Hormone of the Adrenal Cortex (17-hydroxy-11-de-hydrocorticosterone: Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis, Proc. Staff Meet., Mayo Clin. **24**: 181 (April 13) 1949.

Clinical Notes, Suggestions and New Instruments

AGRANULOCYTOSIS FOLLOWING PYRITHYLDIONE (PRESIDON®) THERAPY

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Pyrithyldione (presidon,® 3,3-diethyl-2,4-dioxotetrahydropyridine) is a mild hypnotic and sedative, not a barbiturate derivative, which is now being widely employed. Several reports which recommend its use as a sedative indicate a tendency of the drug to depress the granulocyte count. Koppanyi and others in 1940 noted that in rabbits receiving pyrithyldione by mouth [1] 3 animals exhibited a decrease in the percentage of circulating polymorphonuclear leukocytes from 34 to 11, 24 to 12, and 19 to 9 per cent, respectively. However, the animals survived after the drug was discontinued. An even more significant observation on human subjects was recorded by Polatin and Horwitz in 1947.[2] In a series of 10 patients whose white blood cell counts were carefully followed daily during three weeks' administration of the drug (600 mg. daily), they noted that 1 patient's total white blood cell count dropped from 8,700 to 3,850 with no change in the percentage of polymorphonuclear leukocytes (62 per cent). After a short rest period, the patients were again given 600 mg. of pyrithyldione a day for three more weeks, and again their blood was examined. The patient who had previously manifested leukopenia was lost to follow-up after nineteen days, at which time his white blood cell count had dropped from 6,750 to 5,650. The authors [2] made the suggestion that "there remains the possibility that nine more days of medication might have led to a similar reduction in the white cell count as did the daily administration of 0.6 Gm. over a period of twenty-eight days during the first course. While no leukopenia developed on the second occasion, the possibility cannot be excluded that the first chronic test caused a transient leukopenia in this one case."

The present case is reported because of a severe and complete agranulocytosis apparently related to the administration of pyrithyldione.

REPORT OF CASE

The patient, a man aged 50, previously had been in good health. His past history was noncontributory except for the recurrent use of alcohol for many years. Nevertheless, he was well nourished and took ample rations of vitamins both orally and parenterally. A routine examination several months before his present illness had revealed that the blood count, sedimentation rate and urinalysis were normal. A roentgenogram and cardiogram of the chest revealed normal condition, and the liver was only slightly enlarged. During the past three years this patient had taken various drugs on occasion without any untoward reactions except in one instance. Eight months before his present illness, penicillin that was administered intramuscularly for a prostatic infection provoked a severe allergic type of reaction with urticaria, polyarthritis and angioneurotic edema. Other medicaments which were taken without difficulty both before and after the reaction to penicillin included barbiturates, chloral hydrate, sulfadiazine, bromides, diphenhydramine and tripelennamine.

For about three months before his present illness, the patient had been taking two to three 0.2 Gm. tablets of pyrithyldione a day for nervousness and insomnia with rather satisfactory results. Careful questioning elicited the information that only one other medicament had been used during this time, namely, phenobarbital. The present illness began with a severe sore throat unassociated with fever, cough, upper respiratory infection or pain in the chest. There was at the same time some slight soreness of the gums. Several days later the temperature of the patient rose abruptly to 104 F. The patient was examined at this time, and it was noted that his throat was diffusely red and injected, but without exudate or ulceration. The gums were hyperplastic, somewhat purplish and tender, but without exudate. Physical examination revealed essentially normal conditions except for some enlargement of the submaxillary nodes, which were moderately tender. The blood pressure was 150 mm. of mercury systolic and 100 mm. diastolic. The pulse rate was 120. A throat culture showed the presence of Staphylococcus aureus and a green-producing Streptococcus of the viridans group.

The patient was not given penicillin because of his previous reaction to it; instead, sulfadiazine was prescribed. However, he was severely nauseated and immediately vomited the one dose taken that evening. On the next day examination of the blood revealed a hemoglobin level of 15.4 Gm., red blood count of 5,060,000 and white blood count of 3,000, with 97 per cent lymphocytes and 3 per cent polymorphonuclear leukocytes. The patient was immediately sent to the Presbyterion Hospital, where sedation with pyrithyldione was discontinued and aureomycin therapy was started by mouth. Again he vomited the drug, and after several doses it was discontinued. The patient at this time was acutely and seriously ill, apprehensive and extremely nervous. It was decided to withhold medicaments for forty-eight hours, observing the white blood cell count twice a day in the hope that the patient's own reaction to the infection might provoke a leukocytosis. At this time the white count was 2,200 with 99 per cent lymphocytes and 1 per cent monocytes. The lymphocytes were all mature forms, and there was an apparent increase in the number of platelets on the blood smear. The sedimentation rate was 70 mm. after one hour, and the results of urinalysis were normal. A cephalin flocculation reaction was negative, and the temperature ranged about 103 F. The throat and gums were extremely painful, sore, swollen and tender.

As stated previously, there were only two drugs which the patient had been taking before the present illness; phenobarbital 0.09 Gm. daily, which he had used intermittently for years, and pyrithyldione, which he had been taking for about two to three months in daily doses of 400 to 600 mg. During the two days of observation without medication, his blood count remained about the same, with a complete absence of polymorphonuclear leukocytes. Because of increasing symptoms, it was decided to administer diphenhydramine and penicillin, risking the possible allergic reaction to the latter, since he had had a brisk leukocytosis with his penicillin reaction eight months previously. Accordingly, he was given diphenhydramine hydrochloride, 50 mg. every four hours during the day and every six hours at night, with crystalline penicillin 400,000 units intramuscularly every twelve hours. There was no immediate response, although the oral lesions ceased to increase in severity. On the third day his white blood cell count was 3,250 with 1 per cent polymorphonuclear leukocytes, 87 per cent lymphocytes and 12 per cent monocytes. Two days later the granulocytes increased to 4 per cent, then to 7 per cent that afternoon. By the sixth day the percentage of granulocytes was 16, with 2 per cent myelocytes, and the lesions in the mouth definitely began to recede. At this stage his temperature declined to the normal range, and the patient felt greatly improved. Because of decided agitation and nervousness, administration of phenobarbital was begun in 0.03 Gm. doses every four hours. This did not prevent the reappearance of granulocytes, for in the next forty-eight hours they increased to 31 per cent; two days later they reached normal levels with a total white blood cell count of 10,000. The oral lesions healed completely and the patient was sent home, where subsequent counts were taken and found to be within normal limits.

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1. Koppanyi, T.; Herwick, R. P.; Linegar, C. R., and Foster, R. H. K.: Studies on Pharmacology of 3,3-Diethyl-2,4-Dioxotetrahydropyridin, and 3,3-Diethyl-2,4-Dioxopiperidine, Arch. internat. de pharmacodyn. et de thérap. **64**: 123, 1940.

2. Polatin, P., and Horwitz, W. A.: Clinical Evaluation of New Sedative-Hypnotic (3,3-Diethyl-2,4-Dioxotetrahydropyridine) in Psychiatric Conditions, Psychiatric Quart. **21**: 107, 1947.

CONCLUSIONS

A patient with severe agranulocytosis which presumably resulted from the prolonged ingestion of a new sedative, pyrithyldione (presidon,® 3,3-diethyl-2,4-dioxotetrahydropyridine), is reported. The fact that depression of polymorphonuclear leukocytes has been reported following the administration of this compound to rabbits and man lends support to its role in the causation of the agranulocytosis in this patient. The recovery which took place on discontinuance of the drug, despite combined administration of phenobarbital and penicillin, adds further weight to the interpretation that pyrithyldione was responsible for the agranulocytosis.

FOREIGN BODY IN THE BREAST

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The observation of foreign bodies in the breast is extremely rare. The following case is of particular interest in as much as it offers an unusual problem in the differential diagnosis of tumors of the breast.

REPORT OF CASE

The patient was a housewife aged 38 who had always been in good health with a normal appetite and normal bowel habits. Her menses had been a little irregular for the past eight months. Her husband and three children were living and well. The youngest child was 6 years of age. The patient had nursed the first two children. Her mother died of carcinoma of the breast at 64 years of age, her father of carcinoma of the prostate at 73.

About four weeks before the patient sought medical aid, she felt some discomfort in the right breast and found a lump beneath the nipple. This had not grown in size and was not tender. On careful questioning, she denied any trauma to the breast.

Physical examination revealed a heavy-set woman, 5 feet 8 inches (173 cm.) in height, weighing 216 pounds (98 Kg.). Both breasts were pendulous. Beneath and slightly lateral to the nipple of the right breast, there was a firm nontender mass measuring about 6 cm. in diameter. It was not adherent to the skin or chest wall. The nipple on the affected side was slightly more retracted than that of the opposite side. No discharge was apparent. The skin appeared normal. No masses were palpable either in the axillary or supraclavicular area. The hemoglobin level was 12.6 Gm. per hundred cubic centimeters of blood (81 per cent); the white blood cells numbered 9,050, with 62 per cent polymorphonuclear leukocytes, 37 per cent small monocytes and 1 per cent eosinophils. The temperature was 98.8 F., pulse rate 80 and respiratory rate 20. Roentgenograms of the skull, chest, dorsal spine, ribs and pelvis showed no metastases.

The preoperative diagnosis was carcinoma of the breast. An incision around the lower border of the areola was made for biopsy. The breast manifested grossly the appearance of chronic inflammation rather than cancer. While grasping the incision with a double hook, a "bobby pin" was produced. This was open at an angle of about 150 degrees and showed little evidence of corrosion. The wound was then closed after insertion of a small rubber drain. Biopsy showed only chronic inflammation around a sinus tract. The postoperative course was entirely uneventful.

COMMENT

This case appears to be unique. On reviewing the roentgenogram of the chest, the "bobby pin" could be seen but was thought to be on the clothes. On interrogation, the patient denied all knowledge of how the pin entered the breast. She believed that she must have rolled over on it while she was sleeping soundly.

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RELATION OF RELAPSES IN TYPHOID TO DURATION OF CHLORAMPHENICOL THERAPY

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During the past year much information has accumulated on the use of chloramphenicol (chloromycetin®) in the treatment of typhoid. This confirms the original report of Woodward and others,[1] covering the observations on 10 patients, which clearly indicated that the new antibiotic was of great value in this disease. Continued experience reveals that fever disappears by lysis during the first three or four days of treatment.

Our early observations,[1] as well as those of McDermott and his associates,[2] brought out that relapses of typhoid were common in treated patients. In order to eliminate such occurrences, we have prolonged the course of treatment in persons infected with Salmonella typhosa. Analysis of the results obtained in 44 patients with typhoid who received chloramphenicol therapeutically under our observation has indicated a striking relation between the duration of chemotherapy and the incidence of relapses.

Although our observations are being reported in detail elsewhere,[3] it appeared desirable to summarize certain of them at this time in a preliminary note. Following proof of the clinical diagnosis by the cultivation of S. typhosa from the blood, each of the 44 patients received orally an initial loading dose of 3 to 4 Gm. of chloramphenicol, which was followed by 1 to 3 Gm. daily given in divided doses for a variable period of time. A clinical relapse, with reappearance of bacteremia, occurred in 7 of the 13 patients whose initial course of drug was given for 8 days or less, average duration of therapy 6.9 days. None of the members of another group of 19 patients suffered relapses; this group was comparable to the first in essentially all respects, except that treatment was continued for 9 to 14 days, average 11.2. A third group, consisting of 12 patients, was treated for 14 to 23 days, average 18; relapses did not occur among these patients. The day of disease on which treatment was begun in the three groups averaged 13.5, 13.7 and 20.8, respectively. The total dose of chloramphenicol averaged 20.0, 25.7 and 32.8 Gm. for patients in the respective groups. All patients in the first group who had relapses responded satisfactorily when chloramphenicol treatment was again instituted.

CONCLUSION

These results warrant the following conclusions. Chloramphenicol (chloromycetin®) should be administered in adequate amounts for more than eight days to patients acutely ill with typhoid if relapses of the disease are to be avoided. There appears to be little advantage in continuing treatment for more than fourteen days.

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The work on which this report is based was carried on in the General and Military Hospitals and the Institute for Medical Research, Kuala Lumpur, Federation of Malaya, and in the University Hospital, Baltimore.

From the Department of Virus and Rickettsial Diseases, Army Medical Department Research and Graduate School, and Commission on Immunization of the Army Epidemiological Board, Washington, D. C., and the Department of Medicine, University of Maryland, Baltimore.

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EBERTHELLA TYPHOSA INFECTION OF ARTERIOVENOUS ANEURYSM CURED BY EXCISION

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and
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A case of acquired arteriovenous aneurysm infected by Eberthella typhosa, weakened to the point of rupture and cured by surgical intervention is reported because of its interest and rarity. Although this is the fourth case of infected arteriovenous aneurysm reported in the literature as cured by surgical means, it is the only one in which E. typhosa was the infecting organism. The case history, physical observations, pathologic report, treatment and sequelae are reported herewtih.

REPORT OF CASE

History and Preoperative Data.—P. M., a man aged 30, was admitted to Lakeside Hospital by one of us (C. L. H.), on Nov. 14, 1947 for a febrile illness which clinically and with laboratory examination proved to be typhoid. On physical examination, striking but unrelated observations were a loud continuous hum heard on the left over the upper portion of the chest and axilla, a thrill felt in the left subclavicular and axillary areas and a mass about 2 cm. in diameter, palpable in the left axilla. Some of these abnormalities had been discovered at the time of draft board examinations, and subsequent consultations with specialists had left the patient with the impression that he had congenital heart disease. There was no history to substantiate congenital defects of the heart in infancy and childhood; moreover, there were scars anteriorly and posteriorly on the left upper portion of the chest suggesting trauma. Direct questioning revealed a history of gunshot wound some ten years' previously, followed by transient anesthesia and motor paralysis of the left arm. The patient was told by us that he had an arteriovenous communication between the axillary artery and vein as a result of the wound. He was advised to have surgical consultation with the view of repair as soon as his convalescence from typhoid permitted. Toward the end of his hospital stay, the patient experienced pain in the left arm for a few hours. On the disappearance of this pain he was permitted to go home Dec. 11, 1947.

The patient was readmitted to Lakeside Hospital one week later because of recurrence of pain in the left arm, fever, and swelling and increased heat and redness of the left arm and left subclavicular and pectoral regions. On readmission, the temperature was 38.4 C., the pulse rate 104 and the respiratory rate 20. Blood pressure in the left arm was 104 systolic and 65 diastolic; in the right, 130 systolic and 65 diastolic. The left biceps reflex was absent. There was hypesthesia of the skin of the forearm in the distribution of the medial antebrachial cutaneous nerve. Inspection of the arm and shoulder was as previously noted. There was weakness of motor power. The white blood cell count, which had been normal during the course of the typhoid, was now 20,700 per cubic millimeter with a differential count of 76 per cent polymorphonuclear neutrophils, 17 per cent lymphocytes, 6 per cent mononuclear cells and 1 per cent basophils.

The diagnosis clinically was infected arteriovenous aneurysm developing at the site of the traumatic arteriovenous communication, but the nature of the infecting organism was obscure because blood cultures were sterile and because we had no knowledge of other cases of similar infection with E. typhosa. Because of this uncertainty, a trial with penicillin and with streptomycin and sulfadiazine in conjunction was made but without beneficial effect. On the third hospital day Dr. Claude S. Beck inserted a needle into the mass in the axilla with the aim of evacuating a possible abscess. He aspirated pure blood, which on culture grew E. typhosa. The swelling and pain in the arm and shoulder increased, and the previously described murmur and thrill disappeared. No pulse could be palpated in the arm, which was virtually motionless.

Operative Intervention.—On the eighth hospital day, December 26, operation was performed by Dr. C. S. Beck with the patient under nitrous oxide, oxygen and ether anesthesia. The incision was made from the clavicle to several inches below the shoulder on the arm. The middle third of the left clavicle was resected subperiosteally. A tape was passed under the subclavian artery for emergency use. Next, the pectoralis muscle was split and the false sac of the aneurysm was revealed. It extended up over the deltoid and well under the pectoralis muscles. While the brachial artery was being dissected out, the false sac of the aneurysm, which contained about 300 cc. of old blood clot, ruptured. At this point the true aneurysm ruptured, and bleeding was controlled by occluding the subclavian artery above. The necrotic tissue and infected blood in and around the false sac were sucked out, the axillary artery and vein were ligated proximally and distally to the aneurysm, and the true sac was excised after all feeder vessels were tied off. A large nerve trunk of the brachial plexus was inextricably involved in the calcified wall of the aneurysm. Because of the presence of infection, drains were placed and the pectoralis muscle and skin were approximated with sutures. Three thousand cubic centimeters of whole blood were given intravenously during the operation.

Postoperative Course.—The elevation in temperature and pain in and edema of the arm disappeared almost immediately after operation. Moderately large amounts of turbid serosanguineous fluid drained out of the wound, and cultures of this material yielded E. typhosa until the wound closed on the twenty-second postoperative day. On the twelfth postoperative day a pulmonary infarct developed; the patient was given heparin and dicumarol® and responded well. After operation the arm remained warm but was somewhat cyanotic. There was an immediate but gradual increase in return of sensory perception, but the return of motor power from a point of complete absence was slower. Physical therapy was given three times a week after the closure of the wound.

The arm can now be abducted and rotated at the shoulder and flexed and extended at the elbow and wrist. There is little deviation of the hand. The hand is flat in the palm because of wasting of the thenar and hypothenar muscles, and there is an attitude of slight extension of the proximal phalanges with slight flexion of the distal phalanges. Opponation of the thumb is still absent, and supination of the hand is limited. Tendon transplants in the hand are now being done.

Pathologic Report.—In addition to fragments of blood clot "also received are four irregular fragments of previously opened blood vessel wall, the largest of which measures 5.5 by 5 by 0.3 cm. and the smallest 4.5 by 2 by 0.3 cm. The cut edges of the largest fragment of vessel wall can be arranged to form a sac which is roughly spherical. This sac is 2.5 cm. in diameter with two openings in either pole, the larger measuring 1 cm. in diameter and the other 0.8 cm. in diameter. . . ."

Microscopic Description.—"The wall of the aneurysm consists of dense fibrous connective tissue. . . . In one section there are distinct clumps of bacteria on and between connective tissue fibers adjacent to the lumen of the aneurysm. These proved to be gram-negative bacilli. . . . There is focal calcification of the wall."

Dr. Howard T. Karsner reviewed the slides and submitted the following diagnosis: Mycotic infection of the wall of an arteriovenous aneurysm.

COMMENT

An arteriovenous aneurysm caused by a gunshot wound in the region of the left axilla was discovered in a patient having typhoid. At the end of the course of the typhoid, pain in the left arm, tenderness of the aneurysm palpated in the axilla, swelling and increased heat of the subclavicular and subpectoral regions and of the arm, decreased blood pressure, hypesthesia and paralysis in the arm, fever and leukocytosis suggested that the aneurysm had become infected and altered in size or condition. The region was aspirated and later incised, and an aneurysm at the site of the old traumatic arteriovenous communication was excised together with a section of the axillary artery and parts of the brachial nerve plexus which were inextricably involved. A false sac containing 300 cc. of old blood was removed. Necrotic and infected blood and tissue were

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drained from the surrounding area, which extended from the subclavicular region down the left arm to the elbow.

There seems to be no doubt that the infecting organism was E. typhosa. The patient had just had typhoid, and E. typhosa was cultured from the lesion and from the postoperative drainage material on numerous occasions. Gram-negative bacilli were demonstrated in the connective tissue of the wall of the aneurysm.

SUMMARY

Three instances[1] of excision of infected arteriovenous aneurysms have been reported with cure. All 3 involved streptococcic septicemia with the periodic discharge of organisms into the blood stream to produce a chronic illness.

Our case, the fourth to be reported, differs in its emergent nature and in that the infecting organism was E. typhosa and as such was unique. Stengel and Wolferth[2] in 1923 concluded that in 4 cases of mycotic aneurysm reported prior to that time as being due to E. typhosa, typhoid was not proved. We have not found reference to such cases in the more recent literature.

Surgical excision of the aneurysm and drainage of the surrounding area gave prompt relief and ultimate cure after antibiotic therapy had shown no effect.

The rarity of this case is not the sole reason for its being reported. It seems justifiable to point out the very real threat of this arteriovenous fistula to this patient's life. Although the effects of these fistulas on the mechanics of the cardiovascular system are well known and often constitute an indication for surgical intervention, the need for their repair to avoid infection is less commonly appreciated.

2102 Abington Road.

THE TREATMENT OF ACUTE TYPHOID FEVER WITH CHLOROMYCETIN®

WILMOT D. FOSTER, M.D.
and
ROBERT J. CONDON, M.D.
Portland, Ore.

The antibiotic chloramphenicol (chloromycetin®) was first tested clinically against typhoid in the Federation of Malaya last year. The efficacy of the drug against the organism Eberthella typhosa was established by this investigation.[1] Chloramphenicol is a crystalline substance obtained through the processes of concentration and purification of cultures in liquid mediums of a species of Streptomyces originally isolated by Burkholder and shown by him to possess antibacterial activity.[2] Ehrlich and his associates in the research laboratories of Parke, Davis & Company carried out the studies of the antibiotic activity of this species of Streptomyces which led to the preparation of a compound which was given the name chloromycetin.

The purpose of this report is to further substantiate the observations of Woodward and co-workers.[1] The aforementioned investigation was carried out in an endemic typhoid area; this case may be designated as sporadic. It is by nature comparable, however, to an experimental or laboratory infection, because the patient ingested the typhoid organism in his college bacteriologic laboratory, the culture originally having been obtained from a stool culture of a typhoid carrier. Thus it was possible to determine the exact day and hour of the ingestion of the organism and the onset of symptoms. This aspect of the case coupled with the dramatic response of the organism (proved by blood culture) to chloromycetin makes it interesting and timely.

REPORT OF CASE

History.—Mr. M. L. R., a college student aged 20, entered the hospital on March 22, 1949 because of frequent episodes of chills and fever which had not proved amenable to home care.

The history disclosed that seven days before admission the patient had first noticed fever, headache and loss of appetite, associated with weakness and a feeling of malaise. He consulted the college physician, who found nothing of significance on examination and who prescribed acetylsalicylic acid in tablet form. The onset of severe chills and intermittent fever prompted the youth to consult his family physician, who gave him injections of penicillin on three successive days without amelioration of symptoms. When a burning urination with pain in the flanks and loins developed, the patient was again carefully interrogated and thoroughly examined.

Manner of Infection.—It was then discovered that on March 4 the patient had accidentally pipetted into his mouth supposedly attenuated typhoid organisms in the college bacteriologic laboratory. To his knowledge none had been swallowed, and his mouth had immediately been washed with a popular antiseptic solution. The class instructor had assured him the organisms were "safe to handle and were all dead." His fears allayed, the student had forgotten the incident and had neglected immunization procedures or prophylactic therapy. On obtaining this history it was deemed wise to admit the patient to the hospital immediately with a tentative diagnosis of typhoid.

Past Medical History.—Recurrent episodes of aural infections had been complicated with mastoiditis on one occasion. No history of rheumatic fever, scarlet fever, diphtheria or of other complicated childhood disease was obtained. There was no history of valvular heart disease.

Systemic review revealed only an elaboration of the present illness. Careful interrogation disclosed that there had been no rash during the present illness. A family and social history revealed nothing contributory.

Physical Examination.—The patient was a husky, well developed, muscular white man in apparent distress. He was cooperative and alert but mildly depressed; the skin was flushed, warm, dry and unblemished by rash. The temperature was 104.5 F., the pulse rate was 84 per minute and the blood pressure was 120 systolic and 70 diastolic. The pharynx was mildly injected, and except for the relative bradycardia no other abnormalities were discovered.

Laboratory Data.—Pertinent laboratory work was immediately started; cultures of the urine, stools and blood, routine counts and urinalysis, routine agglutinations, a roentgenogram of the chest and electrocardiogram were ordered. Nursing care emphasized frequent sponge bathing and other antipyretic measures, none of which served to lower the fever appreciably. The temperature ranged between 101 and 105.4 F. with frequent racking chills and a profuse sweat. Fluids and electrolytes were administered as required orally and by vein.

The morning of March 23 revealed a decidedly dicrotic pulse and a pronounced bradycardia. Examination of the blood revealed that the hemoglobin level was 98 per cent, the red cell count 4,670,000 and the leukocyte count 7,300, with a differential count of 50 per cent polymorphonuclear leukocytes, 1 per cent basophils, 26 per cent lymphocytes, 5 per cent monocytes and 10 per cent staff cells. The sedimentation rate (Westergren) was 10 mm. in forty-five minutes. The urine was acid, with specific gravity of 1.017, 2 plus reaction for albumin, no reducible sugar and an occasional hyaline cast. The serologic tests and malarial smears were negative. Agglutination tests revealed a 1:80 titer for E. typhosa, 1:20 for paratyphi A and a 1:10 for paratyphi B. Cultures of the urine and stools did not yield the organisms.

Treatment and Course.—Streptomycin: The spleen became palpable during March 23, and on March 24 it was distinctly palpable 3 cm. below the left costal margin. When on March 25 cultures of the blood revealed a gram-negative rod, the patient was started on streptomycin therapy, 2 Gm. per day in divided

1. Hamman, L., and Reinhoff, W. D. Jr.: Subacute Streptococcus Septicemia Cured by Excision of Arteriovenous Fistula, Tr. A. Am. Physicians **50**: 228, 1935. Tourhoff, A. S.; Lande, H., and Kroop, I.: Subacute Streptococcus Viridans Septicemia Cured by Excision of an Infected Arteriovenous Aneurysm, Surg., Gynec. & Obst. **74**:974, 1942. Lipton, S., and Miller, H.: Streptococcus Viridans Septicemia: Subacute Bacterial Endarteritis of an Arteriovenous Aneursym, J. A. M. A. **126**: 766 (Nov. 18) 1944.

2. Stengel, A., and Wolferth, C. C.: Mycotic (Bacterial) Aneurysms of Intravascular Origin, Arch. Int. Med. **31**:527 (April) 1923.

From the Department of Medicine, St. Vincent Hospital, Portland, Oregon.

The chloromycetin® used in this case was supplied by Parke, Davis & Company.

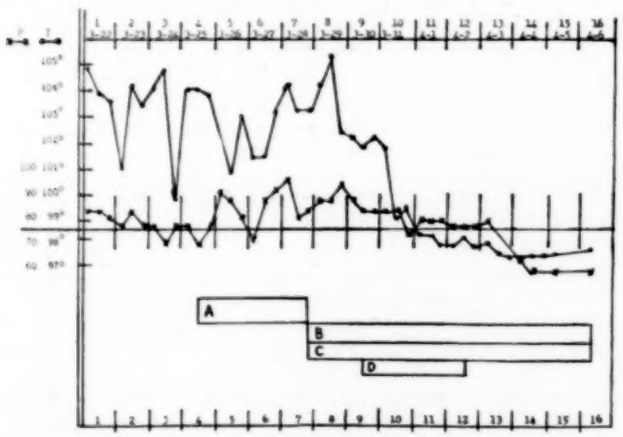
1. Woodward, T. E.; Smadel, J. E.; Ley, H. L., Jr.; Green, R., and Mankikar, D. S.: Beneficial Effect of Chloromycetin in the Treatment of Typhoid Fever, Ann. Int. Med. **29**: 131, 1948.

2. Ehrlich, J.; Bartz, Q. R.; Smith, R. M.; Joslyn, D. A., and Burkholder, P. R.: Chloromycetin: A New Antibiotic from a Soil Actinomycete, Science **106**: 417, 1947.

doses. During the day an uncontrollable diarrhea of liquid green stools commenced.

Streptomycin had no appreciable effect on the disease or the diarrhea. Gradually the bradycardia became more pronounced, as did the dicrotism of the pulse. Heart sounds were somewhat blurred and indistinct. The blood pressure remained stabilized, but the patient lapsed slowly into a stupor and gradually became disoriented and mildly delirious. A transfusion of whole blood on March 26 had no effect on the clinical course.

Chloromycetin: The laboratory reported on March 28 that the organism recovered from the blood was positively identified as E. typhosa. That day a supply of chloromycetin was obtained by air-express. Streptomycin therapy was stopped and the administration of chloromycetin was started immediately, the initial dosage being 3.5 Gm. orally (50 mg. per kilogram of body weight) and a maintenance dose of 0.25 Gm. every two hours. Stupor, fever and carphologia were pronounced the first day of administration and over the subsequent twenty-four hours. Complete orientation and consciousness first returned on March 29. On March 30 the temperature fell abruptly to 102 F. and remained at that level for twenty-four hours. On that day also the diarrhea became controllable and diminished in quantity. Because the patient was bleeding from the nose and because the prothrombin time was low (54 per cent of normal con-



Effect of treatment with (*A*) streptomycin, (*B*) chloromycetin, (*C*) combisul® and (*D*) penicillin on the clinical course of a patient with typhoid.

centration), vitamin K (5 mg. a day) and equal parts of sulfadiazine, sulfathiazole and sulfamerazine (combisul®, 0.5 Gm. four times a day) were given to ward off possible gastrointestinal complications. On March 31 the temperature returned to normal and remained there for the duration of the hospital stay.

However, sonorous and sibilant rales developed in the anterior portion of the left lung; penicillin (50,000 units every three hours) was then administered to abort if possible a complicating pneumonia. These rales rapidly disappeared, and penicillin therapy was stopped on April 2. On this date the persistent and troublesome diarrhea also ceased, and the dosage of chloromycetin was changed to 0.25 Gm. every four hours. The medicament was continued at this rate until April 5, when all treatment was discontinued, the patient having meanwhile become ambulatory. On the next day 3 stool cultures taken during the previous week failed to exhibit growth of typhoid organisms and a negative culture of the duodenal contents was obtained; the patient was then discharged. Agglutination tests on the day of discharge revealed a titer of 1:320 for the O antigen and 1:80 for the H antigen of E. typhosa.

The patient returned to his college studies on April 11 and has remained well to the present.

COMMENT AND CONCLUSION

The course of the disease was uninfluenced by four days of streptomycin therapy, but a complete remission of the fever took place ninety-six hours after the administration of chloromycetin. Two of the 10 patients in the series of Woodward and others [1] relapsed (after 10 and 16 days, respectively) with a bacteremia which reoccurred after an afebrile period. The possibility of a relapse thus was contemplated in this case. However, although the same dosage schedule was used as in the original series,[1] there was no evidence of relapse. It is interesting to note that in the 2 aforementioned relapses, the organisms did not manifest increased sensitivity to the drug in vitro and the recurrent infections responded promptly to a new course of the drug. Tests to determine levels of the antibiotic in the blood or sensitiveness of the organism to the agent were not performed in this case.

It would appear from this case report that chloromycetin® is highly effective in the treatment of typhoid.

AGRANULOCYTOSIS FOLLOWING THE USE OF PYRITHYLDIONE (PRESIDON®)

Results of Diagnostic Test

MORTIMER E. EHRLICH, M.D.
and
LEON N. SUSSMAN, M.D.
New York

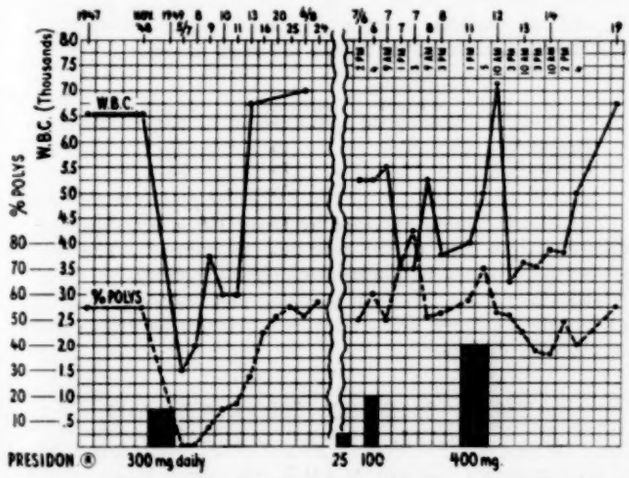
Pyrithyldione (presidon,® or 3,3-diethyl-2,4-dioxotetrahydropyridine) has been widely used since its introduction as a sedative and hypnotic. Its advantages in not being a barbiturate are obvious. The apparent failure to produce any toxic manifestations on the central nervous system, cardiovascular systems, or hemopoietic systems made its use more desirable. Herewith is the first reported case of agranulocytosis resulting from its use. The relation between the administration of the drug and the depressing effect on the granulocytic series is proved by observation of the patient while receiving test doses of the drug.

REPORT OF CASE

M. L., a woman aged 49, works as a promotion executive. Her past history includes a hysterectomy at 36 years of age and an exceedingly labile blood pressure, which responded to emotional strain and overwork by extreme fluctuation. There was no history of allergic diseases. In May 1947 a thorough examination revealed that her heart was normal clinically as well as by roentgenologic and electrocardiographic study. Other laboratory examinations including erythrocyte sedimentation rate, basal metabolic rate, phenolsulfonphthalein excretion, blood sugar, nonprotein nitrogen and cholesterol were within normal limits. The urine was normal, with specific gravity of 1.027. Blood studies revealed 6,500 leukocytes, 55 per cent of which were polymorphonuclear cells. The patient complained of dizziness, fatigue, headache and insomnia which had persisted for several months. Various barbiturates were prescribed. These were found to be mentally depressing. On Feb. 25, 1949 pyrithyldione, 100 mg. three time a day, was prescribed and found to be helpful; it did not cause mental depression or "hangover." The drug was taken irregularly until March 21, when severe pyelitis developed. This responded promptly to penicillin therapy. After this incident greater medical control was instituted, and 100 mg. of pyrithyldione was administered regularly three times a day. After approximately one month (April 29) the patient complained of sore throat, headache, and "stuffed" ears. Two days later her pharyngitis became much severer, and a temperature of 103 F. was noted. There were several postauricular and postcervical lymph nodes which were tender and painful. The nasopharynx was severely injected. Crystalline procaine penicillin G in oil (300,000 units) was injected daily for three days, resulting in a fall in temperature to 100 F., with some resolution of the lymph nodes. Two days later, however, there occurred a pronounced increase in all symptoms and a sudden elevation of the temperature to 103 F. A blood count taken at this time showed a hemoglobin level of 100 per cent, with 4,260,000 erythrocytes per cubic

From medical service and laboratories of Beth Israel Hospital.

millimeter. The total leukocyte count was 1,500, of which 99 per cent were lymphocytes and 1 per cent monocytes. The patient was promptly hospitalized. Pyrithyldione was suspected as the cause of the agranulocytosis. Sternal marrow aspiration performed at this time revealed an extremely active marrow with intense myelocytic proliferation. No mature polymorphonuclear cells were seen. Other cellular elements were present in normal distribution, except for a slight increase in plasma cells. The differential count on the sternal marrow was as follows: myeloblasts 2.5 per cent, promyelocytes 4 per cent, myelocytes 35 per cent, metamyelocytes 5 per cent, lymphocytes 9.5 per cent, plasma cells 5 per cent, normoblasts 39 per cent and no segmented forms. Massive doses of penicillin were given to the patient, who gradually recovered both clinically and hematologically (chart). During the period of hospitalization the patient noted a loss of hair and loosening of the teeth. Her convalescence continued slowly, and she was discharged twenty days after admission. The patient consented to a diagnostic test with pyrithyldione and was readmitted on July 6. Examination of the blood on admission revealed 5,200 leukocytes, of which 58 per cent were polymorphonuclear cells. Gradual doses of the drug were administered, and blood counts were taken at two hour intervals (see chart). On July 6, 25 mg. of pyrithyldione was given. No effect was



Influence of pyrithyldione (presidon®) on the cellular elements of the blood.

noted, and the following day 100 mg. of the drug was administered. Within four hours a fall in the leukocyte count to 3,500 with a rise in the percentage of polymorphonuclear cells from 50 to 84 per cent was noted. After a five day rest period, during which the daily examination of the blood revealed a normal count, two doses of pyrithyldione of 200 mg. each were given. Headache, lassitude, malaise and rise in temperature to 101. F. appeared rapidly followed the next day by a fall in the total leukocyte count to 3,350 and a drop in polymorphonuclear cells to 39 per cent. This persisted for three days; then a gradual rise in the leukocyte count occurred, and all symptoms disappeared. When the white blood cell count had reached normal and the patient was clinically asymptomatic, she was discharged to the care of her physician.

SUMMARY

This case illustrates the depressing action of pyrithyldione (presidon®) on the hemopoietic system and establishes the relation between neutropenia and the administration of the drug. In addition, the occurrence of other toxic effects and complications, such as alopecia and loosening of the teeth, were demonstrated by this patient. The cooperation of the patient and the manufacturer (Hoffmann-LaRoche, Inc.) made these observations possible.

36 East Thirty-Eighth Street.

Council on Pharmacy and Chemistry

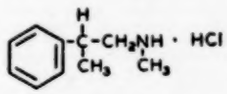
NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

PHENYLPROPYLMETHYLAMINE HYDROCHLORIDE. — Vonedrine Hydrochloride (MERRELL). — *d,l*-1-Methylamino-2-phenylpropane hydrochloride. — $C_{10}H_{15}N \cdot HCl$. — M.W. 185.70. — Phenylpropylmethylamine hydrochloride is made by adding phenylpropylmethylamine to an aqueous solution of hydrochloric acid and is not available in the dry state.

The structural formula of phenylpropylmethylamine hydrochloride may be represented as follows:



Actions and Uses.—Phenylpropylmethylamine hydrochloride, like the volatile base, acts chiefly as a local vasoconstrictor. It is useful in the form of an isotonic solution for topical application to produce shrinking of the nasal mucosa. Its local effects are accompanied with minimal irritation, local tissue reaction or secondary congestion and little or no stimulation of the cardiovascular or central nervous systems. Although relatively nontoxic, ordinary precautions should be observed as for other sympathomimetic agents to avoid the possible untoward effects of overdosage.

Dosage.—Phenylpropylmethylamine hydrochloride is usually applied locally in a concentration of 2.8 per cent, either as drops into the nose, as a nasal spray, nasal tampons, or by displacement followed by suction. Five to 10 drops in each nostril every three hours is usually sufficient to provide symptomatic relief of simple nasal congestion.

Phenylpropylmethylamine hydrochloride is incompatible with silver salts, tannates and picrates.

Tests and Standards.—

Phenylpropylmethylamine hydrochloride solution is clear, colorless and nearly odorless. It has a *p*H of 5.5 to 6.5.

Transfer about 10 ml. of phenylpropylmethylamine hydrochloride solution to a separatory funnel, saturate it with sodium chloride and add 15 ml. of 1 *N* sodium hydroxide. Extract the liberated base with 40, 30 and 30 ml. portions of ether. Wash the combined ether extracts with 10 ml. of water and dry the ether layer for 1 hour over about 10 Gm. of anhydrous sodium sulfate. Filter and evaporate the ether. Take up the remaining liquid in 15 ml. of benzene. If water is still present, add more anhydrous sodium sulfate and decant the benzene onto a filter paper containing anhydrous sodium sulfate. Collect the filtrate in a 25 ml. Erlenmeyer flask. Bubble an excess of dry hydrogen chloride gas through the solution and remove the excess gas by heating on a steam bath. Cool the flask to allow the hydrochloride to separate. Filter and wash the crystals first with dry benzene and then with dry ether, and air-dry with suction. The fine, white crystals are soluble in alcohol, ether and water, and in hot benzene; the compound melts between 147 and 150° C.

Transfer exactly 3 ml. of phenylpropylmethylamine hydrochloride solution to a separatory funnel, dilute with 10 ml. of water, saturate the solution with sodium chloride and add 5 ml. of 1 *N* sodium hydroxide. Extract the liberated base with 40, 30 and 30 ml. portions of ether. Wash the combined ether extracts with 5 ml. of distilled water. Extract the ether solution with exactly 35 ml. of 0.02 *N* sulfuric acid. Wash the ether layer with 10 and 5 ml. portions of distilled water, add the water extracts to the sulfuric acid solution and heat the combined extracts on a steam bath to remove ether. Cool, add 2 drops of methyl red T. S. and titrate the excess sulfuric acid with 0.02 *N* sodium hydroxide. Each ml. of 0.02 *N* sulfuric acid consumed is equivalent to 0.00371 Gm. of phenylpropylmethylamine: the amount of phenylpropylmethylamine hydrochloride is not less than 93.0 or more than 107.0 per cent of the claimed amount.

CETYL PYRIDINIUM CHLORIDE: The cetyl pyridinium chloride in phenylpropylmethylamine hydrochloride solution conforms to the N. N. R. standards for this substance.

PHENYLPROPYLMETHYLAMINE: The phenylpropylmethylamine used in making phenylpropylmethylamine hydrochloride solution conforms to N. N. R. standards for this substance.

THE WM. S. MERRELL COMPANY, CINCINNATI

Solution Vonedrine Hydrochloride, 2.8%: 30 cc. dropper bottles and 473 cc. bottles. Each 100 cc. contains 2.8 Gm. phenylpropylmethylamine hydrochloride, 0.02 Gm. of cetylpyridinium chloride, 0.25 Gm. chlorobutanol and aromatic oils in distilled water. The solution is isotonic, with a *p*H between 5.5 and 6.5.

U. S. trademark 406,970.

PLANTAGO OVATA CONCENTRATE.—Konsyl (Burton, Parsons & Co.)—A preparation consisting principally of the separated outer mucilaginous layers of Plantago ovata seeds (blond psyllium).

Actions and Uses.—Plantago ovata concentrate may be used in cases of simple constipation due to lack of sufficient bulk in the stool. It produces no cathartic action and is, therefore, mainly useful as an aid in chronic constipation, of functional or neurogenic origin.

Dosage.—5 Gm. to 10 Gm. in a glass of water or milk, three times daily, usually before meals, is considered sufficient to promote evacuation of the bowel in most cases. It is important to drink the mixture before it thickens.

Tests and Standards.—

Plantago ovata concentrate is a cream-colored to brown, granular powder, practically odorless and tasteless. Stir 10 Gm. of the powder rapidly into 250 ml. of water: a mucilaginous suspension, containing numerous dark brown discrete particles, is formed. As the hydration and swelling of the mucilaginous portion progresses, the mixture assumes a soft gelatinous consistency.

Transfer 30 Gm. of Plantago ovata concentrate to a suitable flask and determine the moisture content by means of the method for moisture by toluene distillation described in U. S. P. XIII, page 712: the moisture content is not more than 10 per cent.

Add 100 ml. of water to a 100 ml. stoppered graduated cylinder. To the surface of the water, add gradually 1 Gm. of Plantago ovata concentrate, adding the solid sufficiently slowly to prevent the formation of a large clump of wetted solid at the top of the graduate. Stopper the cylinder, shake well, let it stand for 15 minutes and shake again. After 4 hours of standing, the mucilaginous layer at the bottom of the cylinder is more than 30 ml. in volume.

Burton Parsons & Co., Washington 9, D. C.

Konsyl (Powder): 180 Gm. and 360 Gm. cans.

U. S. patent 1,975,731; U. S. trademark 313,620.

Council on Physical Medicine and Rehabilitation

REPORTS OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

Howard A. Carter, *Secretary.*

KOROMEX DIAPHRAGM ACCEPTABLE

Manufacturer: Holland-Rantos Company, Inc., 145 Hudson Street, New York (13).

The Koromex Diaphragm is a contraceptive device consisting of a dome-shaped rubber diaphragm manufactured from natural rubber latex over a cadmium-plated coiled steel spring. The device is available in a series of different sizes, which are specified in terms of external diameter. This diameter ranges from 50 to 105 mm. in gradations of 5 mm. The thickness of the rim is 4.7 mm.

Koromex Diaphragm

In use, the Koromex Diaphragm is guaranteed for two years, and the date of manufacture is stamped on the package. The firm supplied evidence that the shelf-life of the device is at least three years.

The device is used when control of conception is indicated. It is to be used in conjunction with Koromex Jelly or Cream, which have been accepted by the Council on Pharmacy and Chemistry. The firm supplied evidence that the use-life of the device under these conditions is at least two years. Exposure to heat or light or to products containing petrolatum injure the rubber and shorten the use-life. Satisfactory evidence was obtained that the Koromex Diaphragm conformed to the published list of Requirements for Acceptability of Contraceptive Devices.

The Council on Physical Medicine and Rehabilitation voted to include the Koromex Diaphragm in its list of accepted devices.

UNEX MIDGET HEARING AID, MODEL 110, ACCEPTABLE

Manufacturer: Nichols & Clark, Hathorne, Mass.

The Unex Midget Hearing Aid, Model 110, contains microphone, amplifier and batteries in a single metal case. The case measures 17 by 92 by 59 mm. (11/16 by 3 5/8 by 2 5/16 inches). The weights of the various parts are as follows: two batteries, 62 Gm.; receiver and cord, 12 Gm.; case containing amplifier, 64 Gm.; total, 138 Gm. (9 ounces).

Unex Midget Hearing Aid Model 110

The electrical and acoustic data presented by the firm to substantiate the electrical and acoustic performance of the instrument were confirmed by the Council investigator. The voltage of the "A" battery is 1.5; the "A" current is 54 milliamperes. The "B" current is 0.76 milliamperes for 22 volts and 0.40 for 16 volts.

Two subjects, both veteran users of hearing aids, participated in performance tests of these instruments. Discrimination tests with the same 2 subjects were conducted, using phonetically balanced list of 100 monosyllables (recorded version) delivered at 60 decibels and reaching the listeners at 41 and 33 decibels, respectively, above their thresholds for test no. 9. The score for Model 110 is as follows:

	Amplification Without Hearing Aid	Reference Instrument	Model 110	Difference
Subject A	92	85	87	+2
Subject B	94	76	78	+2
			Average	+2

The discrimination provided by Unex 110 is not significantly different from that of the reference instrument. The results of the performance tests are obviously satisfactory.

The Council on Physical Medicine and Rehabilitation voted to include the Unex Midget Hearing Aid Model 110 in its list of accepted devices.

UNEX MIDGET HEARING AID, MODEL 95, ACCEPTABLE

Manufacturer: Nichols & Clark, Hathorne, Mass.

The Unex Midget Hearing Aid, Model 95, contains microphone, amplifier and batteries in a single metal case. It measures 17 by 60 by 92 mm. (11/16 by 2 3/8 by 3 5/8 inches). The weights of the various parts are as follows: two batteries 63 Gm.; receiver and cord, 7 Gm.; case containing amplifier, 62 Gm.; total, 132 Gm. (8 1/2 ounces).

Unex Model 95 is provided with a crystal receiver and has no provision for a magnetic receiver.

Electroacoustic Data.—The data provided by the manufacturer indicate an acoustic gain for Model 95 in the octave from 500 to 1,000 cycles per second. The "A" current is given as 33 milliamperes when the "A" voltage is 1.0, and 41.5 milliamperes for "A" voltage 1.5. "B" current is given as 0.44 milliamperes for 22 volts and 0.20 milliamperes for 16 volts.

Discrimination tests for 2 subjects were performed at levels 35 and 34 decibels, respectively. The performance is better than that of the reference instrument by a margin that is probably significant.

	Amplification Without Hearing Aid	Reference Instrument	Model 95	Difference
Subject A	92	85	90	+5
Subject B	94	76	82	+6
			Average	+5.5

The Council on Physical Medicine and Rehabilitation voted to include the Unex Midget Hearing Aid, Model 95, in its list of accepted devices.

Committee on Cosmetics

The following products have been accepted as conforming to the rules of the Committee on Cosmetics of the American Medical Association. A copy of the rules on which the Committee bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

PEPSODENT DIVISION, LEVER BROTHERS COMPANY

Rayve Creme Waving Lotion.—An aqueous solution of sodium and ammonium thioglycolate containing specified quantities of sodium hydroxide and ammonia. This permits a "cold" wave permanent; its action does not depend on chemically or electrically produced heat. It is particularly adaptable to use in the home if directions are followed carefully.

Rayve Neutralizer.—A pink powder composed of potassium bromate to be used in an aqueous solution following the application of the waving lotion, to neutralize the thioglycolate solution and to fix the wave.

Creme Waving Lotion, 3.75 fluidounces.
Neutralizer, 0.55 ounces.

MARCELLE COSMETICS, INCORPORATED

Marcelle Hypo-Allergenic Cosmetics.—These products are formulated to minimize the possibility of allergic reaction to ingredients. They are scented and unscented.

Face Powder.—Finely powdered, nongritty mineral ingredients with added color and synthetic perfume. It is used to subdue gloss or shine of the skin and conceal minor skin blemishes and imperfections.

Box, 2¼ ounces.

Dusting Powder and Talcum Powder.—Finely pulverized, white, nongritty mineral materials to impart a smooth, absorbent, lightly scented film on the body.

Box, Dusting Powder, 4 ounces; Talcum Powder, 7 ounces.

Cleansing Cold Cream.—A white, creamy, semisolid, emulsion of the beeswax, borax and liquid petrolatum type, to provide emollient and cleansing properties for dry and normal skins.

Jar, 4, 8 and 14 ounces.

Liquefying Cream.—A white, anhydrous material consisting of petrolatum, liquid petrolatum and waxes which melts on contact with the skin. It is used as a cleanser for the oily type of skin.

Jar, 4, 8 and 14 ounces.

Skin Lubricating Cream.—A faintly pink, anhydrous cream consisting of fats and oils chemically similar to normal skin oils in a petrolatum-liquid petrolatum base. It is used for its emollient effect on dry and normal skins.

Jar, 4, 8 and 14 ounces.

Special Foundation Cream for Dry Skin.—A faintly pink, soft, creamy emulsion containing pigments to impart to the dry skin a thin emollient film to which powder will readily adhere.

Jar, 4 and 8 ounces.

Special Foundation Cream for Oily Skin and Vanishing Cream.—A white, pearly, soft, emulsified cream consisting of a stearic acid soap, free stearic acid, water and glycerin. The high water content results in fairly rapid evaporation accompanied with an apparent "vanishing" of the cream. The soap content plus the flexible film of stearic acid remaining on the skin is intended to be effective in increasing the adherence of face powder, especially in the presence of an oily skin.

Jar, 4 and 8 ounces.

Hand Cream.—A pink, moderately soft emulsion containing glycerin, emollient ingredients and water to provide protection for the hands and to give a softer appearance through its emollient action.

Jar, 4 and 8 ounces.

Special Skin Lotion.—A thick white oil-in-water emulsion containing oils and fats in the dispersed phase and glycols in the aqueous phase. It is used to protect and soften the skin.

Bottle, 4 and 8 ounces.

Astringent.—An amber-colored liquid with alcohol as the basic ingredient, with astringent action and solvent activity toward oils. It is used to impart a cool feeling to the skin and to aid in cleansing where there is excessive oiliness.

Bottle, 4 and 8 ounces.

Mild Astringent.—A watery white liquid containing a relatively smaller amount of alcohol and an astringent aluminum salt. It is used for dry skin types and as an after-shaving lotion.

Bottle, 4 and 8 ounces.

Foundation Lotion for Dry and Normal Skin.—A suspension of finely pulverized inert pigments in an emollient oily liquid vehicle. It is used as a powder base to camouflage blemishes and to impart a velvety appearance and even color to the normal or dry skin. It also can be used as a pigmented vehicle for the incorporation of medicaments.

Bottle, 1 ounce.

Foundation Lotion for Oily Skin.—A suspension of finely pulverized inert pigments and other materials in a water-alcohol medium. Fats, oils and waxes are omitted. It is used as makeup for oily skin.

Bottle, 2 ounces.

Lipstick.—A waxy solid of moderately high melting point with a halogen derivative of fluorescein. It is used to enhance the appearance of the lips by added indelible color and to protect against dryness through its emollient properties.

Special Formula no. 372 Lipstick.—This is the same as Marcelle lipstick except that halogen derivatives of fluorescein dyes are omitted. It is a nonindelible lipstick for persons who are sensitive to these dyes.

Lip and Facial Rouge.—This is the same as Marcelle lipstick except softer and creamier in consistency to permit smooth blending on the cheeks.

Special Blend no. 372 Lip and Facial Rouge.—This is the same as lip and facial rouge except that halogen derivatives of fluorescein are omitted.

Dry Rouge.—An intensely colored mixture of mineral ingredients to enhance the color of the cheeks.

Eye Shadow.—A soft waxy material with pigments and color lakes to adjust to various shades. It is used as makeup to enhance the natural shadows at the inner corner of the eyes and accentuate the eyes.

Skin Lubricating Oil.—A faintly pink, anhydrous oily liquid to lubricate the skin.

Bottle, 2 ounces.

Soap.—A white, hard-milled soap essentially composed of tallow to form a bland neutral complexion soap.

Shampoo.—A greenish, opalescent liquid of potassium soaps of vegetable oils.

Bottle, 4 and 8 ounces.

Deodorant.—A white, creamy emulsion containing an aluminum salt to inhibit perspiration in the axillas through an astringent action.

Jar, 1 ounce.

Waving and Curling Fluid.—A pale, brownish mucilagenous liquid containing a gum in an alcohol-water medium. It provides a solution for wetting the hair so that it can be stretched into the "wave" or "curl" configuration and will be held in this position by the adherent film as long as the hair is not exposed to excessive moisture or shampooing.

Bottle, 8 ounces.

Mascara.—Composed of blended waxes and coloring matter to enhance the color of the eyebrows and eyelashes.

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SATURDAY, SEPTEMBER 10, 1949

FINANCING OF HOSPITAL CARE

The modern hospital has evolved from a publicly supported institution which gave institutional and domiciliary care to the poor and unfortunate when they were sick to a complex intricate organization which serves a variety of purposes in the field of health. The hospital has evolved from an institution usually supported by the community or government to one maintained by private agencies and philanthropies and by the fees of persons in the community with the greatest financial resources. Once only the poor went to the hospital when they were sick. Now all classes of people seek the hospital for medical care, including diagnosis, treatment, relaxation and rehabilitation. Modern medicine costs more and is worth far more because of increasing years of life expectancy free from unnecessary suffering. With the advance of medical science at an unprecedented rate, the cost of operation of hospitals has outpaced the sources of individual philanthropy and has extended beyond the ceiling of the ability of most persons to pay for what they receive.

Hospitals serve also as the training centers of great numbers of personnel in the field of health. They fulfil another fundamental function as centers for research in the medical sciences. Many public health activities, including the practice of preventive medicine, are gravitating toward the hospitals. Indeed, the hospital is the focus for the health activities of the community. When the offices of the public health services are associated with the hospital it becomes truly a health center.

The considerations here set forth emphasize the importance of adequate financing for hospitals and at the same time indicate the need for careful study of the factors that enter into the costs of services and the efficiency of the procedures.

Most of the medical care given to the people of the United States in hospitals is provided by the nonprofit voluntary hospital. These institutions serve more than two thirds of all patients admitted to hospitals each year. In 1945 the nonfederal civilian hospitals reported expenditures of 1.4 billion dollars; these same hospitals by 1948 reported expenditures of almost 2.4 billion dollars. The impending financial crisis in the economic situation of the United States, which is approaching the end of four years of inflationary trends, has emphasized the importance of careful consideration of hospital finances. In 1948 one outstanding nonprofit voluntary general hospital reported an operating loss of almost a million dollars. Another similar hospital reported a deficit of $500,000. A majority of the hospitals in Cincinnati have reported an operating deficit of more than $100,000 each for the year. Reports of the American Hospital Association indicate that expenditures in 1948 in nongovernmental general hospitals exceeded income from patients in two thirds of the institutions and expenditures exceeded all income in at least one third of these hospitals. So greatly have costs of care risen in recent years that a large special hospital in Chicago, in which practically all patients pay something and in which a great proportion of the beds are devoted to private patients, shows by its records that not one patient in the hospital during 1949 has paid the cost of the services rendered.

Can patients pay hospital costs? The national average expenditure per patient day in hospitals for short term illnesses during the four year period 1945 through 1948 rose from $8.60 to $13.09. The average cost per day in one state during 1948 exceeded the 1945 average by almost 100 per cent.

During recent years local and state governments and community agencies have been besieged by demands for aid in meeting this critical situation. The process is not a favorable one. Sudden changes in legislation or in municipal or state aid or sudden decreases of income by community agencies might greatly diminish or remove such sources of aid from the conduct of hospitals and thus precipitate a crisis. During the years under consideration voluntary prepayment plans providing insurance against the cost of hospitalization have enrolled many millions of persons. Yet in many instances the insurance does not cover the total of the patient's bill. Patients are astonished and, in such cases, often disturbed when they discover the failure of their insurance to meet the total expenditures. The time has come when an appropriate agency must study the sources of hospital finances, the elements of hospital costs and the entire economics of hospitalization with a view to planning for a sound economic future.

Improvements in medical practice and the advancement of medical science have added greatly to the cost of hospital services. Indeed, the major emphasis in any study of hospital costs may well be placed on the influence of medical practice on the charges made by such institutions. The only effective barrier against

wastage of hospital services and against demands made by patients for unessential services not directly related to medical care is the judgment and cooperation of the attending physician. Methods must be found whereby adequate controls over such demands can be established without jeopardizing the cost and the availability of medical care. Perhaps changes in the organization of hospital services or even in the construction of hospitals would yield economies of time for physicians and patients. The bill which the patient receives may include charges for roentgenologic, clinical, pathologic or laboratory services, drugs and accessories to surgical procedures, which constitute a major portion of the hospital costs. In present circumstances of prepayment for hospital care many beds are utilized by patients undergoing diagnostic study or treatment with physical medicine or psychiatric services who might equally well be kept on an ambulatory basis.

Practically every hospital is today an educational and research institution; many hospitals are equally devoted to preventive medicine and the interest of the public health. These activities contribute inevitably to the size of the patient's bill. Analysis of these costs and proper allocation to responsible agencies may yield reductions in the charges to the individual recipient of hospital care. Study of these factors may result in the provision of more adequate income to hospitals from sources other than the patient himself. Such financing would strengthen the financial economy of the hospital and reduce the costs of care to the individual patient.

Our hospitals are on the threshold of nationwide expansion and the development of new services. The scope of the value of the hospital to the community may be diminished and the advancement of the hospital injured by continuance of outmoded systems of financing hospitals. A comprehensive study of the entire situation is needed immediately; such research should yield more efficient operation, lessened demand for personnel and diminution of cost to the individual patients.

EXPERIMENTAL RUBELLA IN HUMAN VOLUNTEERS

Gregg in 1941 in New South Wales (Australia) established a relationship between the occurrence of maternal rubella and fetal abnormalities. His observations were confirmed by Swan [1] and his co-workers in Australia and by Reese [2] in the United States. Numerous reports from Australia, England and America have confirmed the observation that maternal rubella in the first trimester of pregnancy is responsible for congenital defects such as cataract, deaf-mutism, and congenital heart lesions.

Anderson [3] reports experiments on human volunteers undertaken to demonstrate the feasibility of immunizing girls before marriage and finding a means to prevent infection in vulnerable pregnant women exposed to rubella. The planning of these studies in human volunteers was conducted by the Hall Institute (Melbourne, Australia). The infective material was obtained from throat washings from typical cases of rubella. The material was sealed in ampules at the bedside of the patient, frozen and stored in a mixture of solid carbon dioxide and absolute alcohol. The time taken to obtain the washing from the patient and to store it at —70 C. was no more than five minutes.

Experiments carried out on 40 women volunteers demonstrated that typical rubella could be produced by the inoculation of women volunteers by the respiratory route. The agent responsible remained viable in the presence of 200 Oxford units of penicillin per cubic centimeter, and the evidence suggests that it was filtrable through a millimicron membrane; it is, therefore, probably a virus. The virus was present in throat washings taken on the first day of the rash. The virus remained infective for at least ninety days when stored as frozen throat washings at —70 C. The incubation period, before the appearance of a rash, in human subjects infected by inhalation ranged from thirteen to twenty days. Lymphadenopathy preceded the onset of the rash by as long as six days in some instances. Susceptible persons were infected by contact with the experimental disease. The artificially induced disease did not differ in any way from he natural rubella, and the immunity produced should be equally effective.

Two groups of experiments in which the infective dose employed was obviously large and effective revealed that 14 out of 25 volunteers did not show signs of infection following either the artificial inoculation or subsequent intense natural exposure. Five of these persons gave a history of infection six to nine years previously, and the other 9 probably experienced a subclinical or an unnoticed infection. This in the opinion of Anderson is strong circumstantial evidence that infection provides a high degree of immunity for at least nine years. An artificially induced infection in a woman of 20 could, therefore, be expected to insure immunity over the usual child-bearing period. The possible application of these results to the deliberate infection and immunization of young women as a public health measure will have to take into consideration the existence of a considerable proportion of resistant persons without history of rubella and the dangers of transmission of other infections.

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2. Reese, A. B.: Congenital Cataract and Other Anomalies Following German Measles in the Mother, Am. J. Ophth. **27**: 483 (May) 1944.

3. Anderson, S. G.: Experimental Rubella in Human Volunteers, J. Immunol. **62**:29 (May) 1949.

Current Comment

NEW SOURCE OF SUPPLY FOR CORTISONE

Following the first announcement of the use and value of cortisone in rheumatic diseases came the startling statement that an African plant can be used as a source of supply for this substance. Until recently cortisone was prepared solely from a bile acid. Unfortunately, the product is difficult to manufacture and the supplies even for clinical investigation are so limited that a committee has been formed to aid in the distribution of the drug for research.[1] Many victims of arthritis have requested physicians to use cortisone. Such requests now have increased with the announcement that the African Strophanthus seed may provide more of this scarce remedy. Many problems remain for solution; for example, the species which contain the basic material must be identified, conditions of growth studied and other factors explored. Adequate supplies of cortisone from any source will not be available in the near future, although other sources are being investigated. While awaiting the results of the now intensified research on production of cortisone, let us not forget the great accomplishments of physical medicine in achieving relief in the rheumatic diseases.

HEPARIN INHIBITION OF CELL DIVISION

When a living cell is about to divide, its protoplasm undergoes "mitotic gelation," a sharp increase in viscosity. After the mitotic spindle is formed, the protoplasm reverts to its original fluid state. Since 1928 leading zoologists [1] have assumed that mitotic gelation is similar to the gelation that takes place in the clotting of vertebrate blood. Logically a substance which inhibits blood clotting might also prevent gelation and subsequent cell division. Heilbrunn and Wilson [2] of the Department of Zoology, University of Pennsylvania, have tested this assumption by exposing a number of unicellular forms to heparin or other anticoagulants. The cells thus far tested include paramecia, fertilized sea urchin eggs, frog eggs and eggs of the worm Chaetopterus. In control fertilized Chaetopterus eggs the initial protoplasmic viscosity of 7 increases to 14 on mitotic gelation; the viscosity falls to 7 as soon as the mitotic spindle is formed. Exposure to dilute heparin solution does not prevent fertilization of these eggs, as deduced from the giving off of the first polar body. Mitotic gelation, however, does not take place, the viscosity remaining at 6 or less. In over 70 per cent of the heparinized eggs cleavage does not take place. This inhibitive effect of heparin is not due to a killing action. Washing the eggs several times in sea water causes a twofold increase in the percentage of cleavage. The fact that heparin can prevent cell division was first noted in 1930 by Fischer,[3] who found that dilute heparin added to a tissue culture prevents tissue growth. Fischer's evidence has been confirmed by Paff and others,[4] who succeeded in cultivating mast cells (heparinocytes) from canine livers. They noted that only heparinocytes grew in their tissue cultures. This they interpret as evidence that products elaborated by the mast cells prevent mitosis by other tissue elements. Local secretion of heparin by human mast cells has been demonstrated by Ehrich [5] and his associates of Philadelphia General Hospital. A proposed extension of their studies to sarcoma cells in mice is announced by Heilbrunn and Wilson.

1. Committee of the National Academy of Sciences on the Investigation of Cortisone, editorial, J. A. M. A. **14**: 1158 (Aug. 6) 1949.
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2. Heilbrunn, L. V., and Wilson, W. L.: Proc. Soc. Exper. Biol. & Med. **70**: 179 (Jan.) 1949.
3. Fischer, A.: Virchows Arch. f. path. Anat. **279**: 94, 1930.
4. Paff, G. H.; Bloom, F., and Reilly, C.: J. Exper. Med. **86**: 117 (Aug.) 1947.
5. Ehrich, W. E.; Seifter, J.; Alburn, H. E., and Begany, A. J.: Proc. Soc. Exper. Biol. & Med. **70**: 183 (Jan.) 1949.

ALLERGY IN EPIDEMIOLOGY OF COMMON COLD

Although some yet unidentified virus is generally believed to be the cause of the common cold, the role of contributory factors, such as exposure to cold or fatigue, is still obscure. Fox and Livingston [1] believe that allergy is an important factor in the susceptibility to colds. Allergic conditions, they point out, are frequently initiated or exaggerated by a fall of temperature and increased humidity. The mechanism of this reaction is probably related to increased permeability of a susceptible membrane, allowing the antigen to contact its specific reagin in the cell more readily. The common cold is an allergic response in susceptible persons to contact with a specific protein, which is the cold virus or its products. The diminished capacity to maintain effective circulation and to tolerate sudden fall of temperature exhibited by the cold-susceptible patient is often observed in allergic patients. The response of the allergic person to these environmental factors results in an outpouring of histamine into various shock centers, particularly into the respiratory tract, in sufficient quantity to weaken the local defense mechanism, preparing these tissues for acceptance of the virus of the common cold or of secondary invaders. The authors in 1940 [2] reported a study of 1,200 cold-susceptible persons which revealed that 80 per cent of these persons had various allergies or came from allergic families. In a recent communication [1] these studies embraced over 3,000 persons. The most common pathologic change observed in the upper respiratory tract of cold-susceptible persons is hyperplasia of the mucosal and lymphoid tissues. These patients suffer constantly from postnasal drip and mouth breathing due to nasal intumescence, frequent sore throat, attacks of laryngitis, and stomatitis. The person with hyperplastic tissues highly susceptible to colds rarely has a cold lasting only four to five days. Almost invariably a secondary infection of the sinuses develops, lasting three to six weeks. Apparently, the mucosa must be injured specifically by the virus to cause these long colds. The cold-susceptible patient often presents a borderline or subclinical rather than the frank type of allergy.

1. Fox, N., and Livingston, G.: Role of Allergy in the Epidemiology of the Common Cold, Arch. Otolaryng. **49**: 575-586 (June) 1949.
2. Fox, N.; Harned, J. W., and Pefuse, S.: Borderline Allergy: Its Relation to Hyperplastic Disease of the Respiratory Tract, Arch. Otolaryng. **31**: 502-516 (March) 1940.

ORGANIZATION SECTION

Washington Letter

(From Our Regular Correspondent)

Sept. 6, 1949.

Congressional Group to Study British Health System

Some members of the House Interstate and Foreign Commerce Committee were scheduled to leave Washington September 10 for the British Isles and the Continent to study European health insurance programs. The committee clerk withheld announcement of the itinerary, names of participating committee members and other salient information. Washington writers and commentators commonly refer to such trips as junkets at public expense. Committees, accordingly, disclose only a minimum of information on a visit of this kind. Representative J. Percy Priest, chairman of the subcommittee on health legislation, is not making the trip. Among members of the subcommittee who are expected to make the flight, by military air transport, are Representatives Biemiller, Wilson and Scott. "The committee hopes to secure information that will be helpful in considering legislation now pending before it," said the announcement. The party will go to England, Sweden "and other European countries."

Six Doctors Named to Child Conference Committee

Appointed late in August by President Truman, the National Committee for the Midcentury White House Conference on Children and Youth has six physicians among its membership of fifty-two. The group's first meeting, under the chairmanship of Federal Security Administrator Oscar R. Ewing, was scheduled for September 8-9 at the White House. Appointees include Dr. Raymond B. Allen, head of the Division of Medical Services, Department of Defense, and president of the University of Washington; Dr. Charles Janeway, Boston; Dr. T. Duckett Jones, medical director, Helen Hay Whitney Foundation; Dr. William Menninger, Topeka, Kan.; Dr. Edward B. Shaw, University of California Medical School, and Dr. Benjamin Spock, Mayo Clinic, Rochester, Minn.

CIO'S *Economic Outlook* Attacks A. M. A.

The August issue of *Economic Outlook*, official publication of Congress of Industrial Organizations, is devoted in its entirety to an attack on the principle of voluntary health insurance and a eulogistic presentation of the case for compulsory health insurance. It charges that the American Medical Association "is spreading highly misleading literature about the proposal and has tried to give the impression that doctors would lose the right to take or reject patients and the right to practice as they think best."

Although CIO offices in Washington issued a two page special press release on the article, which is illustrated with cartoons, minimal space was given to the story by the press in the national capital.

U. S. Clinical Research Center

Some of the outstanding features of the $40 million clinical research center being built at suburban Bethesda, Md., by U. S. Public Health Service were described September 4 by Dr. Leonard A. Scheele, Surgeon General. The fourteen story, air-conditioned structure is due to be completed by July 1952.

Chronic and metabolic diseases and certain types of infectious and tropical conditions will be studied and treated at the center. Patients will be selected from all parts of the country, on referral by physicians, hospitals or other medical institutions.

The radiation laboratory will occupy three floors underground and five above. Nuclear research equipment will include a 12 million volt electrostatic generator, a synchrotron and a 2 million volt radiotherapy machine. A 500 seat auditorium is to be fitted for television of surgical and laboratory procedures. Some of the seats will be especially wired for the hard of hearing. An eight room surgical suite will be provided. All anesthesia will be performed by physicians. Other features include a large scientific library, a central sterilization and supply unit, a rehabilitation department, a chapel and such conveniences as beauty parlor, barber shop and circulating library.

Coming Medical Meetings

Ambulatory Fracture Association, Toronto, Canada, Royal York Hotel, Oct. 24-27. Dr. H. W. Wellmerling, 120 S. LaSalle St., Chicago 3, Secretary.

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 9-14. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Clinical and Climatological Association, White Sulphur Springs, W. Va., The Greenbrier, Oct. 27-29. Dr. James Bordley III, Bassett Hospital, Cooperstown, N. Y., Secretary.

American College of Surgeons, Chicago, Stevens Hotel, Oct. 17-21. Dr. Paul B. Magnuson, 40 E. Erie St., Chicago 11, Secretary.

American Hospital Association, Cleveland, Sept. 26-29. Mr. George P. Bugbee, 18 East Division St., Chicago, Executive Secretary.

American Public Health Association, New York, Oct. 24-28. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

American Roentgen Ray Society, Cincinnati, Oct. 4-7. Dr. H. Dabney Kerr, University Hospitals, Iowa City, Iowa, Secretary.

American Society of Clinical Pathologists, Chicago, Drake Hotel, Oct. 11-15. Dr. C. G. Culbertson, 740 S. Alabama St., Indianapolis, Secretary.

American Society of Maxillofacial Surgeons, Montreal, Can., Sept. 11-14. Dr. Casper M. Epsteen, 25 E. Washington St., Chicago 2, Secretary.

Colorado State Medical Society, Denver, Shirley-Savoy Hotel, Sept. 20-23. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver, Executive Secretary.

Conference of State and Provincial Health Authorities of North America, New York, Oct. 28. Dr. Russell O. Saxvik, State Health Officer, Bismarck, N. D., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 10-12. Dr. W. Edwin Bird, 822 North American Bldg., Wilmington, Executive Secretary.

District of Columbia, Medical Society of the, Washington, Hotel Statler, Oct. 17-19. Mr. Theodore Wiprud, 1718 M St. N.W., Washington 6, Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 6-7. Dr. Arthur J. Butt Jr., 1101 N. Palafox St., Pensacola, Fla., Secretary.

Indiana State Medical Association, Indianapolis, Sept. 26-29. Mr. Ray E. Smith, 1021 Hume-Mansur Bldg., Indianapolis 4, Executive Secretary.

Inter-American Congress of Surgery, Chicago, John B. Murphy Memorial Auditorium, Oct. 21-23. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Chairman Program Committee.

Kansas City Southwest Clinical Society, Kansas City, Mo., Municipal Auditorium, Oct. 3-6. Dr. W. Merritt Ketchum, 630 Shukert Bldg., Kansas City, Mo., Secretary.

Kentucky State Medical Association, Owensboro, Oct. 6-9. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.

Michigan State Medical Society, Grand Rapids, Pantlind Hotel and Civic Auditorium, Sept. 21-23. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.

Mississippi Valley Medical Society, St. Louis, Jefferson Hotel, Sept. 28-30. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Ill., Secretary.

Neurosurgical Society of America, Quebec, Canada, Chateau Frontenac, Oct. 17-19. Dr. Edward Schlesinger, 710 W. 168th St., New York, Secretary.

Nevada State Medical Association, Elko, Sept. 29-Oct. 1. Dr. Roland W. Stahr, 118 California Ave., Reno, Secretary.

Oklahoma City Clinical Society, Oklahoma City, Biltmore Hotel, Oct. 24-27. Dr. F. Maxey Cooper, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

Oregon State Medical Society, Eugene, Oct. 12-15. Dr. Werner E. Zeller, Medical-Dental Bldg., Portland 5, Secretary.

Pacific Association of Railway Surgeons, Sun Valley, Idaho, Challenger Inn, Sept. 23-25. Dr. W. T. Cummins, 1400 Fell St., San Francisco, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Hotel William Penn, Sept. 26-29. Dr. W. F. Donaldson, 8104 Jenkins Arcade, Pittsburgh 22, Secretary.

Southern Minnesota Medical Association, Red Wing, Sept. 12. Dr. W. A. Merritt, 102 Second Ave. S.W., Rochester, Secretary.

Southwestern Surgical Congress, Houston, Tex., Shamrock Hotel, Sept. 26-28. Dr. C. R. Rountree, 1200 N. Walker St., Oklahoma City, Secretary.

Virginia, Medical Society of, Fort Monroe, Old Point Comfort, Oct. 9-12. Miss Agnes V. Edwards, 1200 E. Clay St., Richmond, Secretary.

Washington State Medical Association, Seattle, Olympic Hotel, Sept. 11-14. Dr. James W. Haviland, 338 White-Henry-Stuart Bldg., Seattle, Secretary.

Western Orthopedic Association, Santa Barbara, Calif., Biltmore Hotel, Oct. 19-21. Dr. Charles W. Gilfillan, 1680 N. Vine St., Hollywood, Calif., Secretary.

Wisconsin, State Medical Society of, Milwaukee, Hotel Schroeder and Milwaukee Auditorium, Oct. 3-5. Mr. Charles H. Crownhart, 704 E. Gorham St., Madison, Secretary.

World Medical Association, General Assembly, London, Eng., Oct. 10-15. Dr. Louis H. Bauer, 2 E. 103d St., New York City, Secretary General.

Wyoming State Medical Society, Casper, Sept. 12-14. Dr. George H. Phelps, 1606 Capitol Avenue, Cheyenne, Secretary.

PROGRAM OF THE AMERICAN MEDICAL ASSOCIATION FOR THE ADVANCEMENT OF MEDICINE AND PUBLIC HEALTH

A Federal Department of Health

1. Creation of a Federal Department of Health of Cabinet status with a Secretary who is a Doctor of Medicine, and the coordination and integration of all Federal health activities under this Department, except for the military activities of the medical services of the armed forces.

Medical Research

2. Promotion of medical research through a National Science Foundation with grants to private institutions which have facilities and personnel sufficient to carry on qualified research.

Voluntary Insurance

3. Further development and wider coverage by voluntary hospital and medical care plans to meet the costs of illness, with extension as rapidly as possible into rural areas. Aid through the states to the indigent and medically indigent by the utilization of voluntary hospital and medical care plans with local administration and local determination of needs.

Medical Care Authority with Consumer Representation

4. Establishment in each state of a medical care authority to receive and administer funds with proper representation of medical and consumer interest.

New Facilities

5. Encouragement of prompt development of diagnostic facilities, health centers and hospital services, locally originated, for rural and other areas in which the need can be shown and with local administration and control as provided by the National Hospital Survey and Construction Act or by suitable private agencies.

Public Health

6. Establishment of local public health units and services and incorporation in health centers and local public health units of such services as communicable disease control, vital statistics, environmental sanitation, control of venereal diseases, maternal and child hygiene and public health laboratory services. Remuneration of health officials commensurate with their responsibility.

Mental Hygiene

7. The development of a program of mental hygiene with aid to mental hygiene clinics in suitable areas.

Health Education

8. Health education programs administered through suitable state and local health and medical agencies to inform the people of the available facilities and of their own responsibilities in health care.

Chronic Diseases and the Aged

9. Provision of facilities for care and rehabilitation of the aged and those with chronic disease and various other groups not covered by existing proposals.

Veterans' Medical Care

10. Maintenance of existing high standards of medical care for veterans, including extension of facilities where the need can be shown and, where practicable, care of the veteran in his own community by a physician of his own choice.

Industrial Medicine

11. Greater emphasis on the program of industrial medicine, with increased safeguards against industrial hazards and prevention of accidents occurring on the highway, at home and on the farm.

Medical Education and Personnel

12. Adequate support with funds free from political control, domination and regulation of the medical, dental and nursing schools and other institutions necessary for the training of specialized personnel required in the provision and distribution of medical care.

GOVERNMENT SERVICES

ARMY

DR. GRADY APPOINTED SCIENTIFIC DIRECTOR

Brigadier General Raymond O. Dart, director of the Army Institute of Pathology, with the approval of the Surgeon General and on recommendation of the Committee on Pathology of the National Research Council, has announced the appointment of Dr. Hugh G. Grady as the scientific director of the American Registry of Pathology, succeeding Colonel James E. Ash, who is retiring from active participation in the registries.

Dr. Grady received his M.D. degree from Jefferson Medical College in 1934 and served an internship and residency at the Philadelphia General Hospital. He has since been an associate professor at Jefferson Medical College and pathologist at St. Mary's Hospital in Philadelphia and with the National Cancer Institute. During the war he served as pathologist and executive officer of the Army Institute of Pathology. He also served as chief of laboratory service, Winter General Hospital, Topeka, Kan., and the Station Hospital, Camp Carson, Colo., and as commanding officer of the Antilles Department Laboratory, Puerto Rico.

MEDICAL DEPARTMENT RETAINS 300 CIVILIAN INTERNSHIPS

The Army Medical Department will maintain 300 spaces for the current fiscal year in the Civilian Intern Program, which, since its inception last year, has been one of the most effective means of recruiting medical personnel for the Army.

Under the Civilian Intern Program, senior medical students who have been accepted for internship training in a civilian hospital approved by the American Medical Association are invited to apply for commissions in the Medical Corps Reserve. If they qualify, they are commissioned as first lieutenants in the Reserve and complete their internships as officers on active duty, with full pay and allowances. On completion of their internship training, they apply for commissions in the Regular Army Medical Corps.

The Civilian Intern Program is one phase of the Army Medical Department's Graduate Professional Training Program. Another is the Military Intern Program, under which senior medical students who apply and are accepted for Medical Corps Reserve commissions as first lieutenants receive their internship training in an Army general hospital approved by the Council on Hospitals and Medical Education of the American Medical Association.

OFFICERS SELECTED FOR ADVANCED TRAINING

The following additional medical officers have recently been accepted for advanced training by the civilian institutions indicated:

Col. Clifford A. Gray, Mayo Clinic, Rochester, Minnesota, radiology.

Col. Thomas W. Mattingly, Harvard Medical School, Boston, cardiology.

Col. Byron L. Steger, Johns Hopkins University, Baltimore, public health.

Col. Elmer A. Lodmell, University of California Medical School, San Francisco, "Oncology Newer Aspects."

Lieut. Col. Harold S. McBurney, Mellon Institute of Industrial Research, Pittsburgh, "Second Annual Symposium on Orthopedic Appliances."

Capt. Edward F. Gudgel, University of Minnesota, Minneapolis, dermatology.

First Lieut. Albert G. Miller, University Hospitals, Minneapolis, residency in pediatrics.

First Lieut. Jay C. Hoyt, St. Francis Hospital, Peoria, Illinois, residency in medicine.

First Lieut. Henry T. Russell, Jefferson Davis Hospital, Houston, Texas, residency in pathology.

First Lieut. Norman R. Davis, Baltimore City Hospitals, Baltimore, residency in ophthalmology.

First Lieut. Philip H. Philbin, Peter Bent Brigham Hospital, Boston, residency in pathology.

NEW MEDICAL SERVICE CHIEF AT WALTER REED

Col. Paul S. Fancher assumed duty August 16 as chief of medical service, Walter Reed General Hospital, according to Major General Paul H. Streit, commanding general of the Army Medical Center. He succeeded Col. Charles R. Mueller, medical service chief since June 1946, who has been transferred to Murphy General Hospital, Waltham, Mass. For the past two and one-half years Colonel Fancher has been chief of medical service, Percy Jones General Hospital, Battle Creek, Mich.

NAVY

SPECIAL WEAPONS AND RADIOACTIVE ISOTOPES

The Surgeon General, Rear Admiral C. A. Swanson, recently announced the establishment of two new courses of instruction for inactive reserve medical officers in medical aspects of special weapons and radioactive isotopes. The courses will be given under the sponsorship of the medical officer in commend, Naval Medical School, National Naval Medical Center, Bethesda, Md. The first course is scheduled to begin Sept. 26, 1949, and will continue through October 1. The second course is to begin November 10, and will continue through November 19.

Inactive reserve medical officers who desire to attend one of these courses should submit a request for training duty to the commandant of their Naval District. Requests for the November course should reach the commandant's office prior to October 15.

The facilities at the Naval Medical Center make it necessary to restrict the number of attendance of each course to 210. District quotas will be established by the Bureau of Naval Personnel. A limited number of sleeping quarters will be available at the Center to those who wish such accommodations. Full mess facilities will be available.

PHOTOFLUOROGRAPHIC EXAMINATIONS

A total of 262,341 photofluorographic examinations were performed on Navy civilian employees at Navy Medical Department activities in the Continental United States and overseas between March 1948 and June 1949. Five out of every 1,000 persons examined were found to have evidence of tuberculosis which required immediate attention. In addition, 3 out of every 1,000 persons examined were found to have evidence of other diseases within the chest requiring immediate attention, such as lung tumors and heart disease. These persons were not aware of their illness at the time of their examination.

NAVAL HOSPITAL AT ST. ALBANS

Ceremonies at the laying of the cornerstone for the new construction of permanent facilities at the U. S. Naval Hospital at St. Albans, N. Y., were held recently. Rear Admiral C. A. Swanson, the surgeon general and chief of the Bureau of Medicine and Surgery, was one of the speakers for the occasion. Others from the Bureau of Medicine and Surgery who attended the ceremony were: Rear Admiral Joel T. Boone (USN), Rear Admiral C. J. Brown (USN). Capt. L. G. Jordan (USN), Capt. O. H. Alexander (USN) and Lieut. Comdr. A. H. Nelson (USN).

WOMEN DOCTORS TO INTERN IN NAVY HOSPITALS

For the first time in the history of the Medical Department of the Navy, three women doctors, recent graduates in medicine, have been assigned to Navy hospitals as interns. There are seventeen other women graduates in medicine who have been assigned to civilian hosiptals under the Navy's Civilian Intern Training Program. The three doctors assigned to Navy hospitals are:

Lieut. (jg) Suzanne W. Brown, New Market, Va., to the Naval Hospital, National Naval Medical Center, Bethesda, Md. (graduated: Medical College of Virginia).

Lieut. (jg) Hannah H. Pendergast, 1904 Spaulding Street, Boise, Idaho, to the Naval Hospital, Chelsea, Mass. (graduated: Vermont University School of Medicine).

Lieut. (jg) Mary W. Tilden, Jamestown, N. C., to the Naval Hospital, Great Lakes, Ill. (graduated: Medical College of Virginia).

The following doctors (lieutentants, j.g.) were assigned to civilian hospitals:

Helen W. Anderson, 125 South Rolling Road, Springfield, Pa., to the University of Pittsburgh Medical Center Hospitals, Pittsburgh (graduated: Woman's Medical College of Philadelphia).

Ruth M. Allen, 2906 Indian River Road, Norfolk, Va., to Union Memorial Hospital, Baltimore (graduated: Medical College of Virginia).

Eleanor E. J. Bundy, 183 Lamont Drive, Decatur, Ga., to the Medical College of Virginia Hospital, Richmond, Va. (graduated: University of Virginia Medical School).

Barbara J. Call, 9 Oliver Street, Salem, Mass., to Salem Hospital, Salem, Mass. (graduated: Tufts Medical College).

Anna E. Connell, 918 Atkinson Drive, Lufkin, Texas, to University and Affiliated Hospitals, Little Rock, Ark. (graduated: Baylor Medical College).

Julia M. Cullen, 165 Saranac Avenue, Buffalo, to Millard Fillmore Hospital, Buffalo (graduated: University of Buffalo School of Medicine).

Betty J. Kizer, Fairmount, Ill., to Research and Educational Hospital, Chicago (graduated: University of Illinois School of Medicine).

Jacqueline LoGrasso, 513 Prospect Avenue, Buffalo, to Millard Fillmore Hospital, Buffalo (graduated: University of Buffalo School of Medicine).

Margaret L. McGrath, 315 Clearview Avenue, Crafton, Pa., to Philadelphia General Hospital, Philadelphia (graduated: Loyola University School of Medicine).

Elizabeth L. McGee, Bent Road, Bowling Green, Pa., to Hospital of Woman's Medical College of Philadelphia (graduated: Woman's Medical College of Philadelphia).

Virginia M. Norrell, 710 South Chase Street, Wheaton, Ill., to St. Barnabas Hospital, Minneapolis (graduated: University of Illinois School of Medicine).

Sara Jean Parks, 141 East Fairmont Avenue, State College, Pa., to the Medical Center, Jersey City, N. J. (graduated: Hahnemann Medical College).

Patricia L. Pear, 43 Soledad Street, Salinas, Calif., to the Gouverneur Hospital, New York (graduated: Southwest Medical College).

Shirley J. Peterson, 525 North Prospect Avenue, Park Ridge, Ill., to St. Francis Hospital, Evanston, Ill. (graduated: Washington University School of Medicine).

Marion A. Puszcz, 10 Trinity Street, Yonkers, N. Y., to St. Mary's Hospital, Rochester, N. Y. (graduated: New York Medical College).

Mildred V. Tuggle, 1108 Colquett Avenue, North East, Atlanta, Ga., to Hospital of Woman's Medical College, Philadelphia (graduated: Woman's Medical College of Philadelphia).

Irene M. Vrabel, 3-14 34th Street, Fairlawn, N. J., to the Medical Center, Jersey City, N. J. (graduated: Woman's Medical College of Philadelphia).

PUBLIC HEALTH SERVICE

TOUR BY VENEREAL DISEASE EXPERTS

Seven international experts on venereal disease arrived in Washington on August 15 to begin a six week study of United States control centers. The group is sponsored by the World Health Organization and is known as the WHO Syphilis Study Commission. The purpose of the tour is to provide the first international evaluation of American methods of venereal disease control, currently based on rapid treatment with penicillin.

The members of the commission are:

Dr. Juan M. Funes, director, Rapid Treatment Center, Quatemala City, Guatemala.

Dr. E. I. Grin, director, Venereal Disease Dispensary, Ministry of Health, Sarajevo, Yugoslavia.

Dr. N. Jungalwalla, venereal disease adviser to the Government of India.

Dr. Poul V. Marcussen, director, Municipal Venereal Disease Clinic, Copenhagen, Denmark.

Dr. Tauno I. Putkonen, chief of the Venereal Disease Division, Finnish Board of Health, Helsinki, Finland.

Dr. Sidney Laird, Adviser in Venereology, Suffolk, England.

Prof. Pierre Joulia, professor of skin diseases and syphilis, Bordeau University, Bordeau, France.

Dr. P. J. Pesare, medical officer in charge of venereal disease education, Public Health Service, Federal Security Agency, will serve as medical secretary to the commission.

Dr. Leonard A. Scheele, Surgeon General, Public Health Service, said, "The close exchange of technics and methods of treating disease is a basic principle of the work of the WHO. We hope to learn much of value in the control of venereal disease from this group of distinguished experts, and we trust that they will render a full and frank report on their findings so that this nation, as well as other nations, may profit fully from their visit."

After spending a week in Washington, the commission left for Boston; New York; Baltimore; Philadelphia; Chicago; Minneapolis; Hot Springs, Ark.; Atlanta, Ga.; Savannah, Ga., and Chapel Hill, N. C., and will return to Washington the first week in October to participate in the third meeting of the WHO Expert Committee on Venereal Infections at the Pan American Sanitary Bureau on October 10.

SEEK NEW SOURCES OF SUPPLY FOR CORTISONE

While the discovery of cortisone offers great possibilities, the supply at present is limited, and the clinical work necessary to prove the usefulness of this product cannot be done until an adequate supply is available. The manufacturing problem is extraordinarily difficult and expensive.

The United States Public Health Service is launching a program to discover new sources of supply for cortisone and has reason to believe that certain plants of the Strophanthus variety may be a source of supply. An expedition sponsored by the Public Health Service and the Department of Agriculture has been dispatched to obtain specimens of various plants that grow in Africa, Malaya, Liberia and China. The expedition is in charge of Dr. John T. Baldwin of the Department of Agriculture, who will search for plants and investigate the possibilities of cultivating them on a large scale in Liberia as well as the feasibility of transplanting them to the United States. Dr. Erich Mosettig, chemist of the National Institutes of Health, will accompany Dr. Baldwin on preliminary visits to Kew Gardens in London, where certain of these plants are under cultivation, and to the laboratories of Dr. T. Reichstein in Switzerland. The present process of synthesizing cortisone requires thirty-seven steps. There are indications that the process required can be greatly simplified through the use of these plants, permitting a larger and continuous supply at much less expense.

EXAMINATION FOR SANITARIANS (NUTRITIONIST)

A competitive examination for appointment of sanitarians (nutritionist) in the Regular Corps of the United States Public Health Service will be held on Nov. 14, 15 and 16, 1949. Applications must be received no later than October 17.

Appointments will be made in the grade of senior assistant sanitarian (equivalent to Army rank of captain) and are permanent.

Application forms and additional information may be obtained by writing to the Surgeon General, United States Public Health Service, Washington 25, D. C. Attention: Division of Commissioned Officers.

COURSE IN DIAGNOSIS OF RABIES

The Communicable Disease Center of the U. S. Public Health Service, 605 Volunteer Building, Atlanta 3, Ga., announces a one week course in the Laboratory Diagnosis of Rabies, November 14-18. The course is open to all grades of employed laboratory personnel without tuition fee. Travel and living expenses must be paid by the individual or his employer. A list of hotels and rooming houses will be sent to applicants at the time of their acceptance for the course by the medical director in charge of the course at the aforementioned address.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

Surgeons' Meeting.—The Southern California Section of the U. S. Chapter of the International College of Surgeons will hold a clinic day program in the auditorium of the Los Angeles County Medical Association September 14. The guest speaker at the dinner at the Hotel Mayfair will be George W. Beadle, Sc.D., chairman of the Division of Biology, California Institute of Technology, Pasadena, whose subject will be "Genes, Enzymes and Viruses."

Courses in Poliomyelitis.—The National Foundation for Infantile Paralysis has made a grant to aid the first of a series of short courses on care of poliomyelitis patients. The first course will be offered November 7-11 at the Orthopaedic Hospital in Los Angeles and will cover the problems of the patient from onset to optimum recovery. The course is particularly recommended for orthopedists, pediatricians and general practitioners who desire an orientation in the over-all care of the patient. Courses for registered nurses and physical therapists will be given from November 7-18. For information address Charles L. Lowman, M.D., 2400 South Flower Street, Los Angeles.

CONNECTICUT

Personal.—Dr. Fred C. Green, New Haven, has been appointed by Governor Bowles to a six year term as a member of the State Tuberculosis Commission. He received his medical degree at Meharry Medical College, Nashville, in 1941, is a graduate of Howard University, Washington, D. C., and has practiced in Connecticut since 1946.

Hospital News.—Construction has begun on a 200 bed general hospital to cost $3,500,000 which is being built by the Greenwich Hospital Association. It is scheduled for completion next fall. Although at first the capacity will be 200 beds, the hospital services are designed to accommodate 300 persons. The three major and three special operating rooms and delivery rooms will be air conditioned.

INDIANA

University Appointment.—Dr. Herbert S. Gaskill, associate in psychiatry of medicine at the University of Pennsylvania School of Medicine, Philadelphia, has been appointed professor of psychiatry at the Indiana University School of Medicine, Bloomington-Indianapolis. Dr. Gaskill, a graduate of the University of Pennsylvania, 1937, serves as a consultant in neuropsychiatry to the Surgeon General's office.

New Mental Multimillion Dollar Hospital.—Cornerstone ceremonies were held July 24 for the $2,000,000 main building and administration unit of the Northern Indiana Hospital at Westville. About one third of the thirty buildings planned for the $22,000,000 mental hospital are already under construction. The hospital will accommodate 1,500 patients by June 1951. It will increase by 30 per cent the state's present facilities for about 9,000 mental patients. According to Mr. Isadore E. Levine, LaPorte, chairman of the board, the hospital will be the first in the nation to handle both civil and criminal mental patients on the same premises. It will accommodate 650 criminals in need of mental care who are now housed in the State Prison at Michigan City.

KENTUCKY

Dr. Eller Appointed Head of Department.—Dr. C. Howe Eller, Richmond, Va., has been appointed head of the department of preventive medicine and public health at the University of Louisville School of Medicine and director of the Louisville-Jefferson County Health Department. He is a graduate of the University of Colorado School of Medicine, 1930, and has been a member of the School of Hygiene and Preventive Medicine, Johns Hopkins University School of Medicine, Baltimore. The Louisville-Jefferson County Health Department combines its services with the Louisville General Hospital, State Tuberculosis Sanatorium and the Medical School.

Employee Health Survey.—An employee health survey set up by Kentucky industries is being conducted by the state department of health to obtain information from each plant regarding its doctors, nurses or first aid attendants, medical examinations, laboratory or first aid quarters, rules on physical examinations, plans for future medical programs and employee health needs. The purpose of the survey, which will be completed in two months, is to provide statistical data to interested agencies for use in planning full time county health setups, to insure effective use of state and local public health services and to provide a mailing list for distributing information on public health.

MAINE

Board of Registration of Medicine.—At the regular July meeting of the Maine Board of Registration of Medicine, Dr. Magnus F. Ridlon, Bangor, was elected chairman and Dr. Adam P. Leighton, Portland, secretary. This is Dr. Leighton's thirty-fifth year as a member of the board. Dr. Paul D. Giddings of Augusta was appointed by Gov. Frederick G. Payne to replace Dr. Roland L. McKay of Augusta. Dr. Seth H. Read, Belfast, was reappointed for a six year term.

Dedicate New Laboratory Buildings.—The Hon. Harold L. Ickes and Surgeon General Leonard A. Scheele, Washington, D. C., spoke at the dedication ceremonies of the reconstructed Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine, on the occasion of the laboratory's twentieth anniversary, August 21. Ceremonies took place on the first floor of the nearly completed main wing of the new laboratory which replaces the units destroyed during the forest fire of 1947. Visitors looked down on the group of modern summer school buildings donated and dedicated last year by the Ladies Auxiliary to the Veterans of Foreign Wars. The laboratory's restored library, which will be housed in this wing, was officially dedicated on August 3 and was also a gift of the Ladies Auxiliary. Other events scheduled include the remainder of scientific lectures by outside scientists which started on June 21, a reunion of staff members and guest investigators and special open house days. In announcing the dedication ceremonies, Dr. Clarence C. Little, who in 1909 started what is now the oldest strain of inbred mice, now in its two hundred and nineteenth generation, said: "Jackson Laboratory today is bigger and stronger than ever before. There are larger stocks of mice on hand at the laboratory now than at the time of the fire, when 90,000 were wiped out. Our own scientists are still working in improvised quarters, which will house new stocks of mice when the main unit is completed." The new buildings, started on May 6 of the year following the fire, consist of four three-story wings of brick, concrete and aluminum and will house experimental animals, the basic pure strains which are distributed to all the laboratories, facilities for the resident staff of investigators and their assistants and working space for a number of visiting scientists for all-year-round use. There will be special laboratories for biochemistry, bacteriology, tissue culture and other special technics. The total construction cost of the new buildings, including the summer research center donated by the Ladies Auxiliary, is $955,000. A grant from the Rockefeller Foundation covered the cost of unit 1 and part of unit 2. The federal government, through the National Cancer Institute, has contributed $350,000. The remainder has been gained through grants from philanthropic foundations and contributions from the Jackson and Webber families and a large number of persons all over the country.

MINNESOTA

Public School Medical Report.—The annual report of the Minneapolis Public Schools Health Service, released on July 16 by Dr. Hermina H. Hartig, chief school physician, showed that 15,934 Minneapolis school children were examined in 1948-1949, an increase of 5,000 over the previous year. The eight physicians who gave part time service to the schools detected eye and ear defects in about 12 per cent of the children. The physicians discovered 560 cases of malnutrition and 230 cases of athlete's foot. The commoner communicable diseases were found in the same incidence as in previous years, but the number of poliomyelitis cases went from 5 in 1947-1948 to 66 in 1948-1949. The report revealed that 15 per cent of Minneapolis public school pupils have not been immunized against smallpox and that 6 per cent have not been immunized against diphtheria.

MISSISSIPPI

Dr. Underwood Honored.—Dr. Felix J. Underwood, state board of health director, was honored August 8 on his twenty-fifth anniversary as health officer for the state. At the meeting, presided over by Dr. Henry Boswell, a member of the state board of health, Dr. Underwood received a scroll bearing more than a hundred signatures and a new Buick sedan given by many friends.

MISSOURI

Personal.—Dr. Leo Wade, formerly assistant professor of medicine and preventive medicine, Washington University School of Medicine, St. Louis, resigned July 1 to become associated with the medical department of the Standard Oil Company of New Jersey.

Kansas City Clinical Conference.—The Kansas City Southwest Clinical Society will hold its annual fall clinical conference at the Municipal Auditorium, Kansas City, October 3-6. Out of state speakers include:

Edgar V. Allen, Rochester, Minn., Clinical Use of Anticoagulants.
Harry E. Bacon, Philadelphia, Diverticulitis of the Sigmoid: Indications for Surgery.
Grayson L. Carroll, St. Louis, Urinary Infections—Their Treatment.
Oscar T. Clagett, Rochester, Minn., Indications for Pulmonary Resection.
Ralph W. Danielson, Denver, Ocular Conditions in Children.
Aubrey O. Hampton, Washington, D. C., Benign and Malignant Ulceration of the Stomach.
Lewis M. Hurxthal, Boston, Diagnosis of Angina Pectoris.
Frank H. Lahey, Boston, Antithyroid Agents in Thyroid Disease.
Virgil H. Moon, Winston-Salem, N. C., Fluid Balance in Health and Disease.
Walter L. Palmer, Chicago, Treatment of Intractable Ulcer.
John L. Parks, Washington, D. C., Pathology of Pregnancy.
Isidore S. Ravdin, Philadelphia, Recent Advances in Preoperative and Postoperative Care.
Wolfgang W. Zuelzer, Detroit, Anemia in Infancy and Childhood.

Round table luncheons will be held daily, and a clinicopathologic conference will meet Monday evening. There will be scientific and technical exhibits.

NEBRASKA

State Association to Review Complaints.—The Council on Professional Ethics, designed as a self-disciplinary body, was set up at the annual meeting of the state medical association last May in Omaha. The council has announced that it is prepared to review complaints brought by patients against doctors who are members of the state association. The house of delegates of the association has established procedures by which complaints against doctors will be judged. Members of the council are Drs. Morris Neilsen Blair, chairman; John R. Kleyla, Omaha; George E. Charlton, Norfolk; Charles F. Heider, North Platte, and Karl S. J. Hohlen, Lincoln.

NEW MEXICO

State Medical Election.—The New Mexico Medical Society at its recent meeting elected the following officers for the coming year: Drs. James W. Hannett, Albuquerque, president; I. J. Marshall, Roswell, president-elect, and Harold L. January, Albuquerque, secretary-treasurer. Six members of the New Mexico Medical Society were appointed to honorary membership by the house of delegates at the annual meeting in May. The newly appointed members are: Drs. Charles W. Gerber, Las Cruces; Frederick F. Doepp, Carlsbad; William W. Phillips, Roswell; Alexander P. Horwitz, Roswell; Homer A. Stroup, Artesia, and Chester Russell, Artesia. Zalmon E. Funk, Santa Rosa, is the only other honorary member of the society.

NORTH CAROLINA

Memorial Infirmary.—Gardner-Webb College, Boiling Springs, will offer medical care to college students and residents of the area at its S. S. Royster Memorial Infirmary to be opened in October. Provided from a fund started by the late Dr. Stephen S. Royster of Shelby and supplemented by his family, the infirmary will be completed by the community and staffed for twenty-four hour service. It is a one story T-shaped structure containing twelve beds, offices for the college physicians and nurses, x-ray equipment, diathermy facilities and a small diagnostic laboratory. The college hopes to be able to cooperate with county and state health agencies in providing preschool clinics, blood tests for syphilis, immunization, chest roentgenograms, home visits by nurses, Red Cross blood donations and an educational program in health.

PENNSYLVANIA

New State Mental Health Department.—Dr. Hilding A. Bengs, assistant director of the Bureau of Mental Health in the Pennsylvania State Department of Welfare since 1944 and director since 1946, has been named state commissioner of mental health. Dr. Bengs had for twelve years been on the Warren State Hospital staff before entering public health work. The position of state commissioner of mental health is a newly created post.

Annual Graduate Institute.—The Third Annual Graduate Education Institute of the Medical Society of the State of Pennsylvania will open October 3 with sessions in the following cities: Allentown, Clearfield, Erie, Harrisburg, Johnstown, Lancaster, Oil City, Reading, Scranton, Washington and Williamsport. A large faculty of medical teachers will hold ten full day seminars, five in the fall and five in the spring. More than 300 lecturers from the medical schools in Pennsylvania will take part in this program.

Philadelphia

Bequest to Medical College.—The Women's Medical College of Pennsylvania at Philadelphia has been bequeathed $10,000 in the will of the late William S. Meade of Haddon, Conn. Mr. Meade is a former Wesleyan University professor.

Personal.—Dr. Chevalier Jackson, professor of bronchoesophagology at Temple University School of Medicine, Philadelphia, was awarded an honorary fellowship by the Royal College of Surgeons at the International Congress of Otolaryngology in Edinburgh, Scotland, on July 26.

SOUTH CAROLINA

Society News.—The South Carolina Surgical Society was organized in Charleston June 23 with Dr. George H. Bunch, Columbia, as president. Dr. William C. Cantey, Columbia, was elected secretary-treasurer.

Piedmont Postgraduate Assembly.—The annual Piedmont Postgraduate Assembly will be held September 20-21. Included in the program are:

Edgar A. Hines Jr., Rochester, Minn., Diagnosis of Peripheral Vascular Diseases.
John R. McCain, Atlanta, Ga., Management of Prolonged Labor.
Calvin B. Stewart, Atlanta, Ga., Cancer of the Female Genital Organs.
Paul B. Beeson, Atlanta, Ga., The Newer Antibiotics.
Clyde F. Bowie, Anderson, S. C., Management of Injury to the Urinary Tract.

Panel discussions of chest injuries; burns and shock, and fractures will be held Wednesday afternoon at 3 p. m.

TEXAS

University Appointment.—John C. Finerty, Ph.D., associate professor of anatomy at Washington University School of Medicine, St. Louis, has been appointed associate professor of anatomy at the University of Texas Medical Branch, Galveston. Dr. Finerty received his professional training at the University of Wisconsin, Madison, and became a Rackham Foundation Fellow at the University of Michigan, Ann Arbor, in 1942. He has been associated with Washington University School of Medicine, St. Louis, for the past few years.

Clinical Pediatrics Meeting.—The Texas Pediatric Society will hold its annual clinical meeting at the Gunter Hotel, San Antonio, October 7-8. Guest speakers include:

Charles A. Janeway, Boston, Recent Advances in Common Communicable Diseases.
Edith L. Potter, Chicago, Treatment of Erythroblastosis.
Wallace S. Sako, New Orleans, Pediatric Emergencies.

Physicians not members of the Texas Pediatric Society will pay a registration fee of $10, which includes luncheon and banquet tickets.

VIRGINIA

State Medical Meeting.—The Medical Society of Virginia will hold its annual meeting at the Chamberlin Hotel, Fort Monroe, October 9-12. Guest speakers include:

R. Lomax Wells, Washington, D. C., Present Day Concept of Industrial Medicine.
Wilburt C. Davison, Durham, N. C., Sir William Osler—Reminiscences.
Herbert Acuff, Knoxville, Tenn., World Medical Association.
Marcus M. Ravitch, Baltimore, Total Colectomy and Anal Ileostomy.
Arthur T. Hertig, Boston, Causal and Preventive Aspects of Spontaneous Abortion.

WEST VIRGINIA

Committee on Hospital Relations.—A special committee on hospital relations authorized by the annual meeting of the West Virginia State Medical Association has been named. Dr. Robert J. Wilkinson of Huntington is chairman and the other members are Drs. Cecil O. Post, Clarksburg, and Robert J. Reed Jr., Wheeling. The committee will attempt to settle the differences which arise among hospitals, hospital managements, and the professional staff at the state level, provided these controversies cannot be settled at the local county level under the broad general principles of the Code of Ethics of the American Medical Association.

GENERAL

Academy of Sciences Meeting.—The National Academy of Sciences will hold its autumn meeting in the Strong Auditorium at the University of Rochester, Rochester, N. Y., October 25-26. The award of medals by the academy will be made at the banquet at 7:30 p. m. October 24 in the Hotel Seneca.

Society for the Crippled.—Nearly $6,000,000 was contributed through the 1949 Easter Seal campaign for service to the nation's handicapped, the National Society for Crippled Children and Adults reports. Among the services the national society and its member units provide for the nation's handicapped are cerebral palsy services and clinics, consultation and organizational services to cerebral palsy parent groups, consultation in speech, occupational and physical therapy, employment services for the handicapped and many other activities. These are supported almost entirely by Easter Seal contributions. More than 90 per cent of the funds raised annually remain in the state in which they are contributed.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the National Office of Vital Statistics, U. S. Public Health Service.

Division and State	Week Ended Aug. 27, 1949	Week Ended Aug. 22, 1948	Median Expec.	Jan. 1 to Aug. 27, 1949	Jan. 1 to Aug. 28, 1948	Total* March 19-Aug. 27, 1949	Total* March 20-Aug. 28, 1948
New England States:							
Maine	44	5	2	224	15	224	15
New Hampshire	32	..	5	89	7	89	7
Vermont	10	5	2	42	13	40	12
Massachusetts	194	21	27	737	86	737	83
Rhode Island	15	..	1	50	..	50	..
Connecticut	70	7	7	235	53	232	52
Middle Atlantic States:							
New York	573	87	105	2,575	500	2,555	464
New Jersey	122	50	36	506	265	530	258
Pennsylvania	65	47	47	269	260	250	249
East North Central States:							
Ohio	123	76	50	721	474	715	465
Indiana	58	19	16	624	157	614	147
Illinois	276	62	62	1,522	358	1,506	351
Michigan	282	53	53	1,301†	221	1,281†	215
Wisconsin	81	31	26	415	151	401	151
West North Central States:							
Minnesota	183	89	57	911	367	872	339
Iowa	102	57	19	589	328	576	315
Missouri	116	21	10	817	106	806	106
North Dakota	50	5	7	289	27	285	27
South Dakota	25	10	1	166	72	144	72
Nebraska	51	54	18	256	278	243	273
Kansas	33	18	8	395	110	369	107
South Atlantic States:							
Delaware	4	5	5	29	90	27	89
Maryland	16	7	9	74	29	65	28
District of Columbia	7	12	12	41	49	40	49
Virginia	34	31	20	163	261	153	259
West Virginia	18	7	7	204	66	197	61
North Carolina	13	133	17	150	1,750	123	1,735
South Carolina	10	28	5	65	235	52	227
Georgia	15	18	7	109	138	101	137
Florida	6	5	4	141	164	120	147
East South Central States:							
Kentucky	33	8	8	293	108	285	105
Tennessee	31	18	18	303	182	297	175
Alabama	12	17	7	146	118	133	106
Mississippi	19	9	6	214	79	208	77
West South Central States:							
Arkansas	50	7	2	716†	80	705†	84
Louisiana	10	9	4	145	75	133	69
Oklahoma	62	25	7	821	220	814	214
Texas	69	71	34	1,606	1,256	1,515	1,235
Mountain States:							
Montana	2	3	3	25	28	24	18
Idaho	33	3	1	269	81	256	54
Wyoming	9	9	2	61	54	61	54
Colorado	53	4	7	273	44	271	42
New Mexico	14	7	3	92	45	91	43
Arizona	13	14	6	95	61	84	60
Utah	12	4	4	91	34	75	31
Nevada	..	..	..	10	2	10	1
Pacific States:							
Washington	48	12	12	258	108	213	90
Oregon	15	3	6	97	58	81	42
California	101	226	24	1,229	1,877	940	1,845
Total	3,214	1,412	.....	20,513†	11,155	19,597†	10,805
Median, 1944-1948			1,412	7,792		7,529	

* Last two columns show reported incidence since approximate average seasonal low: 23 weeks.

† Corrections (deducted from cumulative totals): Michigan: weeks ended August 6, 1 case; August 13, 2 cases; August 20, 1 case. Arkansas: weeks ended July 30, 2 cases; August 20, 1 case.

American Hospital Association.—This organization will hold its annual convention in Cleveland September 26-29 with headquarters at the Statler Hotel. Subjects under discussion include cooperation of voluntary enterprise and government, each maintaining its status, hospital service which organized labor desires, technical aspects of hospital departmental functions, financing and distribution of hospital care, quality of hospital care and organization for it and supervision within the hospital. The annual banquet will be held Thursday evening. The women's auxiliaries of the association will meet in conjunction with the association.

Funds for Mental Health Program.—The Josiah Macy Jr. Foundation has made a grant of $45,000 to the World Federation for Mental Health to help finance the federation's mental health program adopted recently in Rome. The grant is to be given over a period of three years. The first year $15,000 is given unconditionally, and the grants for the other two years are given on condition that the federation raise at least $60,000 a year from other sources. The federation, founded last year in London by the International Congress on Mental Health, estimates it needs $120,000 annually to set up offices in Geneva and arrange meetings.

Congress of the International Society of Surgery.—This congress will be held in New Orleans October 10-15 under the presidency of Prof. G. Grey Turner, London, England. The program includes:

Surgery and Pathology of the Pancreas, Especially in Relation to Its Endocrine Function, Dr. Ian Aird, London.
Surgery of the Parathyroid Glands, Dr. Paolucci, Rome.
Surgery of the Suprarenal Glands, M. R. Fontaine, Strasbourg.
Pathology and Surgery of the Pituitary Gland, M. Paul Martin, Brussels.
Treatment of Postoperative Thrombosis and Its Sequelae, Alton Ochsner, New Orleans, and Michael E. DeBakey, Houston, Texas.
Causes of Recurrence after Operations on the Biliary Tract, M. R. Demel, Vienna.

Dr. Steigman Joins National Foundation.—Dr. Alexander J. Steigman is currently serving as full time consultant in clinical epidemiology for the National Foundation for Infantile Paralysis. Dr. Steigman recently completed a two year period as senior fellow in pediatrics, National Research Council, during which time he conducted investigations in poliomyelitis at the Children's Hospital Research Foundation in Cincinnati. His temporary departure from pediatrics will be for the purpose of field work in early diagnosis, management and epidemiologic investigations of poliomyelitis. He has been associated with the pediatric department at the University of Pennsylvania and Harvard and Temple universities.

CORRECTION

"Action of Procaine on Sulfonamide Compounds."—In the Query and Minor Note with this title in THE JOURNAL, July 23, page 1068, it was stated that procaine splits into triethanolamine and para-aminobenzoic acid. This was erroneous. Procaine is hydrolized into diethylaminoethanol and para-aminobenzoic acid.

The So-Called "Cerebral Palsy" Program.—In the letter to the Editor in THE JOURNAL, Aug. 13, 1949, on page 1232, the last sentence in the left hand column should read: "The eternal cycle of changing therapeutic measures in those crippled children's problems which result from disease of the central nervous system is sufficient proof that we as clinicians and orthopedists have more difficulty with these problems than with any other."

Marriages

CHARLES EUGENE MAY, Jackson, Ala., to Miss Patricia Ann Holland of Bowling Green, Ky., in Nashville, Tenn., June 18.

JAMES TINDALL QUATTLEBAUM, Columbia, S. C., to Miss Grace Wilbur of Newberry, July 16.

SPIROS P. SARRIS, Lowell, Mass., to Miss Aphrodite Valos of Evanston, Ill., in Chicago, July 23.

WILLIAM IACONETTI, Oakland, Calif., to Miss Lorraine Olsen in San Francisco, July 9.

GEORGE A. BLAKESLEE to Mrs. Nadine Rubans Bandler, both of New York, July 15.

RICHARD Y. WESCOAT to Miss Lucy Grace Gaddy, both of Raleigh, N. C., July 1.

ROBERT E. FLYNN, Albia, Iowa, to Miss Marion Kelleher of Des Moines, June 11.

Deaths

Dr. Irvin Abell ✠ Louisville, Ky.; former president of the American Medical Association, died August 28, aged 72, of heart failure while on a fishing trip in Canada. Dr. Abell was born in Lebanon, Ky., Sept. 13, 1876. He received his A.M. degree from St. Mary's College, St. Mary, Ky., in 1894 and his M.D. degree from Louisville Medical College in 1897. The following year he did graduate work at the University of Berlin and the University of Marburg, Germany. Since 1900 he practiced in Louisville, where he was on the staff of the Louisville General Hospital and of St. Joseph's Infirmary and a consultant at Children's Free Hospital and Kosair Crippled Children Hospital.

Dr. Abell was a member of the faculty of the University of Louisville for nearly forty-nine years, serving eight years as assistant in surgery, as professor of surgery from 1908-1923 and as clinical professor of surgery until 1947, when he became professor emeritus. He was also a trustee of the university.

In the American Medical Association Dr. Abell served as a member of the House of Delegates at the annual sessions 1922, 1924-1928 and 1930-1935. From 1931 until 1937 he was a member of the Council on Scientific Assembly and for two years served as its chairman. He was president of the American Medical Association from 1938-1939 and in 1940 was appointed chairman of its Committee on Medical Preparedness.

Irvin Abell, M.D.

Dr. Abell was a specialist certified by the American Board of Surgery. He was a fellow of the American College of Surgeons and had been a member of the Board of Regents since 1926 and chairman since 1939. He was a member of the Board of Governors 1925-1928, president of the college in 1946-1947 and president and chairman of the board of directors of the Franklin H. Martin Memorial Foundation. He was a past president of the Southern Surgical Association, Southern Medical Association, American Urological Association, American Gastro-Enterological Society, Southeastern Surgical Congress, the Association of Military Surgeons of the United States and the Kentucky State Medical Association. He was also chairman of the state association's Ephriam McDowell Memorial Committee that purchased the McDowell home in Danville, Ky., and aided in its restoration. He held memberships in the American Surgical Association and the American Society for Control of Cancer and was an honorary fellow of the Royal College of Surgeons.

Dr. Abell was a member of the Surgical Committee of the National Research Council from 1943 to 1946 and was chairman in 1945 of the National Foundation for Infantile Paralysis' committee on a training program for physical therapists and chairman of its general advisory committee. At the time of his death he was chairman of the Committee on Inter-American Relations for the forthcoming Inter-American Congress of Surgery. He was director of the Commonwealth Life Insurance Company, the Fidelity and Columbia Trust Company and the Louisville Foundation. During World War I he was a lieutenant colonel, commanding Base Hospital No. 59, then colonel in the Medical Reserve Corps and commanding officer of the U. S. Army Reserve Corps Hospital No. 59.

Dr. Abell held honorary Sc.D. degrees from the University of Louisville, University of Kentucky at Lexington, Georgetown University, Washington, D. C., and Manhattan College, New York, and honorary LL.D. degrees from Marquette University, Milwaukee, and the University of Cincinnati. In 1938 the University of Notre Dame awarded Dr. Abell the Laetare Medal as an outstanding Catholic layman.

By those who knew him Dr. Irvin Abell will be remembered as a soft-spoken, cultured, learned gentleman, who achieved leadership wherever he chose to affiliate himself. His ability as a surgeon was recognized by his surgical colleagues; his ideals and idealism were known to all the medical profession; he never sought an office, but great responsibilities were constantly placed upon him. Such men are rare in medicine as in other walks of life. The memory of Dr. Irvin Abell will survive the passing of the years.

John William Amesse ✠ Denver; born in Eagle River, Mich., Jan. 15, 1874; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; since 1945 professor emeritus of clinical pediatrics at the University of Colorado School of Medicine; specialist certified by the American Board of Pediatrics; vice president of the American Medical Association, 1943-1944, and member of the House of Delegates from 1930 through 1938; past president of the Colorado State Medical Society, charter member of the American Academy of Pediatrics; member of the American Public Health Association; past president of the Denver Public Health Council and the Denver City and County Medical Society; served in Spanish-American War, in the Marine Hospital Service, later in the U. S. Public Health Service, seeing service in the Philippines and later as the first health officer of Havana, Cuba, under the American Occupation; one of the physicians in charge of combatting the yellow fever epidemic in New Orleans in 1905; received citation for service in France and England during World War I; during World War II chairman of the procurement and assignment committee for physicians, dentists and veterinarians in Denver; for two years on the state board of health; served on the staffs of the Children's, St. Joseph's, Colorado and Denver General hospitals; died August 21, aged 75, of coronary thrombosis.

Robert Edgar Adair, Cartersville, Ga.; Southern Medical College, Atlanta, 1890; member of the American Medical Association; vice president of the Bank of Taylorsville; died June 17, aged 83, of arteriosclerosis.

James Hoffman Bentson, Rochester, Minn.; University of Minnesota Medical School, Minneapolis, 1943; member of the American Medical Association; fellow in surgery at the Mayo Foundation; served during World War II; died in New York June 28, aged 31, of carcinoma.

Etta Charles, Anderson, Ind.; St. Louis Woman's Medical College, 1895; member of the American Medical Association; served as president and secretary of the Madison County Medical Society; formerly on the staff of St. John's Hospital, where she died July 16, aged 87, of chronic congestive heart failure.

Homer Dickens, DeWitt, Ark.; University of Tennessee College of Medicine, Memphis, 1914; member of the American Medical Association; past president of the Arkansas County Medical Society; died in Little Rock June 6, aged 56.

Spencer Augustus Folsom ✠ Orlando, Fla.; Emory University School of Medicine, Atlanta, 1917; formerly secretary of the Florida East Coast Medical Society; fellow of the American College of Physicians; served during World War I; past president of the Orange County Medical Society; on the staffs of Florida Sanitarium and Hospital and Orange Memorial Hospital; died June 26, aged 54, of coronary thrombosis.

Victor P. Genge, Fort Walton, Fla.; Tufts College Medical School, Boston, 1916; served during World War I; formerly health officer of Lafayette County, Miss., Lake County Health Department, Tavares, and in charge of the Highlands-Glades Health Unit; died July 20, aged 54, of coronary occlusion and acute glomerular nephritis.

Max Wolper, New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1888; died June 22, aged 85, of senility.

Foreign Letters

DENMARK

(From Our Regular Correspondent)

COPENHAGEN, Aug. 7, 1949.

Longevity and Mortality Rate of Danish Doctors

V. A. Fenger and J. Nielsen have studied the longevity and mortality of Danish physicians in four periods. The first is from 1908 to 1915; the second during the decade 1925-1935, and the next two, from 1935 to 1939 and 1940 to 1944. The deaths in all these periods are classified in age groups of five years each.

In the first period, i. e., from 1908 to 1915, the average life of a doctor aged 25 was three years shorter than that of the general population of that age. This difference was reduced to one and a half years in the period 1940-1944. In this period the expectation of life of a doctor who had reached the age of 75 was a trifle longer than that of a 75 year old in the general population. It is noteworthy that in the general population and at all ages in Denmark the expectation of life is considerably better than that of the white population in the United States. There is a corresponding but not so pronounced difference between Danish and American doctors. Like their American colleagues Danish doctors have a lower tuberculosis, cancer and accident mortality rate than the male population as a whole. But Danish doctors have a high suicide rate, and their mortality rate from heart disease is more than 40 per cent higher than that of the corresponding general population. Fenger and Nielsen have worked out a table which shows how a variety of diseases, such as syphilis, diabetes and pneumonia, affect the Danish doctor as compared with Danish laymen of the same age. This study is in many repects comparable to the one by Dublin and Spiegelman on American physicans. The two studies permit comparison between Danish and American doctors.

BCG Vaccination

BCG vaccination is carried out more extensively and systematically in Denmark than in any other country. Convincing evidence for this procedure may be found in a statistical analysis by Dr. T. V. Hyge. His investigations were begun in the spring of 1943 when a fulminating outbreak of tuberculosis occurred in a national school for young girls. Since then he has published his observations on their fate from time to time; his latest communication published in *Ugeskrift for Laeger*, May 19, 1949, brings up to date an observation period of several years. The girls were divided into two groups, tuberculin positive and tuberculin negative from the outset. The negative reactors were grouped according to whether or not they had been vaccinated with BCG. Among 105 originally tuberculin-positive girls exposed to infection there were 4 in whom mild pulmonary tuberculosis developed. Among 106 originally tuberculin-negative girls exposed to infection and vaccinated with BCG there were only 2 in whom pulmonary tuberculosis developed. Among 94 originally tuberculin-negative girls exposed to infection and not vaccinated with BCG there were 70 who became tuberculin positive, and among them were 41 showing signs of tuberculosis.

Knud Faber's Autobiography

The recent publication of the personal recollections of Professor Knud Faber, who soon will be 90 years of age, provides in readable form the history of medicine in Denmark for more than half a century. This book is written as a supplement to Faber's earlier book, "Mit Universitetsliv." With characteristic modesty, he has addressed the present book as a personal greeting to friends and old pupils. As more than half of the doctors in Denmark are former pupils, his readers will represent a wide and appreciative circle.

Included in Faber's earlier research were studies on tetanus and diseases of the stomach and blood. His studies of anemia brought him international recognition. Half a century ago he was appointed chairman of the State Tuberculosis Commission, and thereafter the organization of the campaign against tuberculosis in Denmark was largely his work. Within a few years the first public sanatoriums were begun. At present the tuberculosis stations throughout the country are insuring BCG vaccination of every Dane from the second year of life. This well may be regarded as a reflection of Faber's pioneer work. In 1908 he was designated to reorganize the public health service of Denmark, which required diplomacy as well as administrative experience. In earlier days the school at Copenhagen was Denmark's sole university. Faber advocated the creation of a second university, in Aarhus, and eventually the University of Aarhus was established.

Registration of Drug Addicts

The registration of drug addicts by the public health authorities has been suggested to control their supply of drugs. In the Aarhus district there now is cooperation with the doctors to achieve such control. When a drug addict is discharged from a hospital, the hospital authorities give his name and address to the doctors in the district with a note concerning his drug requirements.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, Aug. 4, 1949.

Psychoses and Neuroses in Industrial Workers

Industrial workers of the city of São Paulo are all associates of the Instituto de Aposentadoria e Pensões, a semiofficial organization which furnishes medical care, financial benefits, retirement and pensions. According to a report recently published by Dr. Francisco Tancredi, head of the Division of Neuro-Psychiatry of the Medical Department of the Instituto, among 1,542 associates who sought financial benefits and retirement during the years 1940 to 1945, he was able to find 1,143 cases of psychoses and neuroses. Apparently half of the patients were affected with neuroses not needing hospitalization. The remaining patients presented psychotic symptoms and required hospitalization. Dr. Tancredi points out that of the 1,143 patients only 347 of those with psychoses needed hospitalization, the remaining 796, or practically 70 per cent, being attended at clinics with good possibilities of rehabilitation.

Campaign Against Leprosy

According to a recent release from the Division of Leprosy of the National Department of Health, there are in Brazil, 37,541 persons with leprosy under control; 3,258 were found during 1948. The total number of cases of the disease is estimated at about 50,000, or approximately 78 per 100,000 population. Of the 37,541 patients, 21,546 are interned in thirty-nine leprosariums; the others report to ninety special clinics where they are being treated. The states most active in discovery of new patients are São Paulo, Minas Gerais, Amazonas, the Federal District, Pará, Goyaz and Paraná. Of the 3,258 patients found in 1948, 1,345 had the contagious form of the disease, 1,264 noncontagious and 149 still unclassified. On the basis of the total number of cases known at present, the states with higher incidence are Amazonas, Minas Gerais, Pará, São Paulo, the Federal District, Espirito Santo and Paraná.

The states in which the largest percentages of patients with leprosy are interned in leprosariums are Pará (88.7 per cent),

Amazonas (79.5 per cent), São Paulo (76.5 per cent), Paraná (62.0 per cent), Ceará (51.6 per cent) and Minas Gerais (43.6 per cent). There are 3,019 healthy children of diseased parents interned in twenty-seven preventoriums, 38.4 per cent of these children having been interned immediately after birth and 61.6 per cent after having lived for some time with their parents. The federal government in 1948 spent $1,523,750 to cooperate with the states in the work against leprosy, a part of this sum having been used for the construction of leprosariums and another part for the maintenance of clinics and preventoriums.

Correspondence

ESTIMATION OF URINARY SODIUM

To the Editor:—My attention has been called to a letter in THE JOURNAL of August 6, page 1172, criticizing the article "Estimation of Urinary Sodium: A Simple Test For Patients on Low Sodium Diets" (J. A. M. A. **140**:670 [June 25] 1949). The letter states, "Certain misconceptions and questionable features should be discussed publicly, lest they aid in perpetuating ideas and practices now considered out of date."

The features pointed out by the correspondent are obvious but are inappropriate to the particular article. The test for the estimation of urinary sodium was proposed for two reasons: (1) because of its simplicity and (2) because clinical trial in our opinion has proved its value. That it is for use by the patient and is only a rough approximation of the urinary sodium with a "large error" was reiterated in the article several times. Furthermore, there is no implication in the article that this procedure be used for the "study of sodium metabolism." Workers in the field of electrolyte metabolism are well aware of the inaccuracies entailed in using chloride values as a precise index of the sodium ion, but there is much excellent old and new data demonstrating that under ordinary conditions a parallelism exists between the urinary excretion of sodium and that of chloride. Despite the large error involved, clinical experience with this simple test, under the conditions described in the article, continues to confirm its great practical value.

J. MARION BRYANT, M.D., Ann Arbor, Mich.

RATE OF BLOOD FLOW THROUGH NEEDLES

To the Editor:—In their article on the rate of blood flow through needles (THE JOURNAL, Aug. 6, 1949, page 1145), Brew and Dill quote Poiseuille's law to prove that the radius of the needle used in blood transfusions is of much greater importance than the pressure applied to the transfusion system in hastening the rate of flow. Their solution to the problem of massive transfusion required in serious hemorrhage and shock cases is therefore rather simple—to use a 15 gage needle.

The use of a large needle would be the solution if the obstruction to flow in these serious clinical instances resided in the needle. However, the needle plays a minor role in the gravely diminished rate of transfusion encountered in the treatment of deeply shocked persons. The chief cause of obstruction to transfused blood is a contracture of the venous smooth muscle fibers. This cause is generally recognized but is unfortunately described by the passive and inaccurate term of "collapsed veins." That "contracted veins" is the correct term for the state of the venous system in shock is apparent to anyone who has attempted to force blood into a vein using an ordinary hand syringe in a shocked patient. Great force will often be necessary. It is on these occasions that the ordinary drip methods practically fail. Moreover, the force necessary to push the piston will vary during the procedure. The introduction of about 50 cc. of blood under pressure may be followed by temporary venous relaxation. As the blood pressure of the patient rises, it will be found that less force becomes necessary. Similarly, should the patient die during transfusion from irreversible shock, there will be a full relaxation of the vein a few minutes before death, and blood will pour into it as rapidly as desired from the regular drip apparatus.

Many physicians have used the 15 gage needle for blood transfusions and have still been faced with obstacles to speedy blood replacement. The needle used routinely by the Emergency Medical Service of Great Britain in the last war was even larger than our 15 gage needle, but the same phenomenon of transfusion at a snail's pace was frequent.

Methods to overcome the obstruction to transfusion in cases of shock and hemorrhage should therefore be directed to the chief site of resistance—the vein of the recipient. The solution has not yet been reached but will probably depend on paralyzing the vasoconstrictor nerves to the vein employed.

NORMAN M. HORNSTEIN, M.D., Buxton, N. C.

OPERATIVE OR NONOPERATIVE PROCEDURES FOR UTERINE FIBROIDS

To the Editor:—Reference is made to the article "Operative Vs. Nonoperative Procedures for Uterine Fibroids," by Robert T. Frank (J. A. M. A. **140**:1001-1008 [July 23] 1949). In this article Dr. Frank advocates supravaginal hysterectomy in the treatment of fibromyomas of the uterus, mainly because he never has seen carcinoma arising in the stump. This doctrine is too dangerous to be left uncontradicted. In the material of our comparatively small hospital in the last two years we have treated forty-three histologically proved carcinomas of the cervix, seven of which arose in cervices left after supravaginal hysterectomy. While this material may not be statistically significant, it shows that the remaining cervical stump represents a definite danger to life, and this danger should be weighed carefully against the local discomfort encountered in a certain percentage of patients who have undergone complete hysterectomy.

Herrin, Ill.

FREDERICK P. BORNSTEIN, M.D.,

BLACK TONGUE

To the Editor:—The article "Black Tongue Associated with Penicillin Therapy," by Samuel A. Wolfson, M.D., which appeared in THE JOURNAL (**140**:1206 [Aug. 13] 1949) states that the author had found no reference to this condition in American journals. This disorder was described by me under the title "Black Tongue" in Conn's "Current Therapy" (Philadelphia, W. B. Saunders Company, 1949), wherein it was pointed out that black tongue may be precipitated by the use of penicillin orally, which seems to upset the biologic balance of organisms in the mouth, allowing chromogenic bacteria or fungi to multiply.

Sutton and Sutton, in "Diseases of the Skin" (ed. 10, St. Louis, C. V. Mosby Company) reported a similar observation by Burgheim, who noted black tongue following the administration of sulfanilamide to a patient with gonorrhea, which disappeared when treatment with this drug was discontinued.

CLARENCE SHAW, M.D., Chattanooga, Tenn.

OBITUARY ANNOUNCEMENTS OF DR. RUFFIN AND DR. TAYLOR

To the Editor:—I am indeed surprised at the brevity of the the necrologies of two outstanding doctors, namely, Sterling Ruffin of Washington, D. C., and Alonzo E. Taylor of Palo Alto, Calif. Sterling Ruffin was one of Woodrow Wilson's physicians—and much more—while Alonzo Englebert Taylor was an outstanding American physiologist and food scientist.

Dr. Taylor was a member of the referee board appointed by a president of the United States, professor of physiologic chemistry of the University of Pennsylvania, professor of pathology and physiologic chemistry of the University of California, director of the Food Research Institute at Leland Stanford and a member of the Hoover Commission, in the capacity of special aid to the chief and a connecting link between the Department of Agriculture and the Food Administration. During, and in the aftermath of, the first World War, Dr. Taylor studied and learned about food conditions in Germany as no other American has, and his observations constituted the basis for some of the government reports.

LEWIS WILLIAM FETZER, M.D., Dallas, Texas.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY, INC. *Oral.* Denver, Oct. 16-20. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 27.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY, INC.: *Oral.* Cincinnati, Oct. 21-23. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 17. Asst. Sec.-Treas. Dr. W. A. Werrell, 1 Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Final date for filing applications is Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Part I.* Various Centers. Feb. 3. Final date for filing application is Nov. 5. Sec., Dr. Paul Titus, 1015 Highland Bldg. Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, Oct. 15-19; Boston, April. Sec., Dr. Edwin B. Dunphy, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY. *Part II,* New York City, Feb. 9-10. Address: Sec.-Treas., Dr. Harold A. Sofield, Room 1856, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 4-7. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 7-8. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis.

AMERICAN BOARD OF PEDIATRICS: New York City, Oct. 21-23; Chicago, Dec. 9-11. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec.-Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Parts I and II.* New York, Oct. 22-24. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: November. Sec., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC. *Special Examination.* Chicago, Oct. 24-25. December, New York City. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Cincinnati, Sept. 28-Oct. 2. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, October 26. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* December. *Oral and Clinical.* Chicago, Feb. 11-15. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 18.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ARKANSAS: * *Examination.* Little Rock, Nov. 3-4. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

COLORADO: * *Endorsement.* Denver, Oct. 4. Sec., Dr. George H. Gillen, 831 Republic Building, Denver.

CONNECTICUT: * *Examination.* Hartford, Nov. 8-9. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven.

DELAWARE: *Examination.* Dover, Jan. 10-12. *Reciprocity.* Dover, Jan. 19. Sec., Dr. J. S. McDaniel, 229 State Street, Dover.

DISTRICT OF COLUMBIA: * *Examination.* Washington, Nov. 14-15. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: * *Examination.* Jacksonville, Nov. 27-29. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GEORGIA: *Examination.* Atlanta, Oct. 11-12. *Reciprocity.* Atlanta, Oct. 13. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

IDAHO: Boise, Jan. 9. Exec. Sec., Mr. Armand L. Bird, 305 Sun Building, Boise.

ILLINOIS: Chicago, Oct. 4-6. Supt. of Registration, Mr. Fred W. Ruegg, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 5-7. *Reciprocity.* Des Moines, Oct. 3, Nov. 7, Dec. 5. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 8-9. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

MAINE: Portland, Nov. 8-9. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MARYLAND: *Examination.* Baltimore, Dec. 13-16. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1. *Homeopathic. Examination.* Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 West 40th St., Baltimore.

MINNESOTA: * Oct. 18-19. Sec., Dr. Julian F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Sec., Dr. Felix J. Underwood, State Board of Health, Jackson 113.

MISSOURI: *Examination.* Jefferson City, October 24-26. *Reciprocity.* Jefferson City, October, 23. Exec. Sec., Mr. John A. Hailey, State Capitol Building, Jefferson City.

MONTANA: Helena, Oct. 3-5. Sec., Dr. Otto G. Klein, First National Bank Bldg., Helena.

NEVADA: Carson City, Nov. 7. Sec., Dr. George H. Ross, 112 N. Curry St., Carson City

NEW JERSEY: Oct. 18-21. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 10-11. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NEW YORK: *Examination.* New York, Albany, Syracuse and Buffalo, Oct. 4-7. Sec., Dr. Jacob L. Lochner Jr., 23 S. Pearl St., Albany 7.

NORTH CAROLINA: *Endorsement.* Asheville, Oct. 17. Sec., Dr. Ivan Proctor, 226 Hillsboro Street, Raleigh.

OHIO: *Examination.* Columbus, December. *Endorsement.* Oct. 2. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: *Endorsement.* Portland, Nov. 4-9. Exec. Sec., Mr. Howard I. Bobbitt, 608 Failing Building, Portland.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

PENNSYLVANIA: *Examination.* Philadelphia or Harrisburg, January. Acting Sec., Mrs. Marguerite G. Steiner, 351 Education Buliding, Harrisburg.

RHODE ISLAND: * *Examination.* Providence, Oct. 6-7. Chief, Mr. Thomas B. Casey, 366 State Office Building, Providence.

SOUTH CAROLINA: *Examination.* Columbia, Nov. 8-9. *Reciprocity.* First Monday of every month. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Sioux Falls, Jan. 17. Sec., Dr. C. E. Sherwood, 300 First National Bank Building, Sioux Falls.

TENNESSEE: * *Examination.* Memphis, Sept. 28-29. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

VIRGINIA: *Examination.* Richmond, Dec. 2-3. *Reciprocity.* Richmond, Dec. 1. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WEST VIRGINIA: *Examination.* Charleston, Oct. 3-5. *Reciprocity.* Charleston, Oct. 3. Director, State Health Department, Dr. N. H. Dyer, Room 639, Capitol Building, Charleston.

WISCONSIN: * *Examination.* Madison, Jan. 10-12. Sec., Dr. C. A. Dawson, River Falls.

WYOMING: Cheyenne, Oct. 3. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, Sept. 20. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, Oct. 4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

CONNECTICUT: New Haven, Oct. 8. Executive Assistant, State Board of Healing Arts, Miss Mary G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: Washington, Oct. 24-25. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Nov. 5. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Oct. 14-15. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing 15.

MINNESOTA: *Examination.* Minneapolis, Oct. 4-5. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 4-5. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: Portland, Dec. 3. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: Vermillion, Dec. 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WASHINGTON: Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: Milwaukee, Sept. 24 and Dec 3. Sec., Prof. W. H. Barber, Ripon College, Ripon.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospitals: Liability For Negligence Of Nurse.—This was an action against the defendant hospital to recover damages for injuries sustained by the plaintiff while she was a patient therein, the injuries alleged to have resulted from the negligence of one of the nurses employed by the hospital. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Mississippi.

The plaintiff charged that an agent of the defendant hospital, while acting as attendant and circulating nurse in the operating room, negligently fastened the plaintiff's feet to the operating table by the use of straps in such manner that the blood circulation in the plaintiff's feet was cut off and that she was kept in such position for such a length of time that her feet were seriously and permanently injured. The injuries consisted of two gangrenous sores, one on the outside of each foot below the ankle. The plaintiff's evidence showed that her feet were entirely normal when she went into the operating room, that they were strapped for about forty-five minutes during the operation, that the straps were not loosened during that time, that the plaintiff was removed to a private room in the hospital after the operation and that when she came out from under the influence of the anesthetic about two hours later her feet were hurting. This was about 1 p. m. About two hours later a special nurse, privately employed by the plaintiff's husband, on complaint that the feet still hurt, placed a hot water bottle to the bottom of the plaintiff's feet. This nurse testified at the trial that the hot water bottle was not hot enough to cause a burn. The plaintiff testified that she was conscious at the time and that she felt no discomfort from the heat of the water bottle. This was the only time that a water bottle was applied to her feet. Not long after this a bluish purple spot appeared on the outside of each foot, where the gangrenous sores later developed, and by the end of the day there was fluid underneath the skin at each spot. The attending nurse testified that these places did not appear to be burns and that they were very slow in responding to treatment.

The circulating nurse testified that she had no independent recollection of having been in the room during the operation but that the hospital chart showed that she was there and was acting as circulating nurse on this operation and that the chart was correct. The circulating nurse handles things that are not sterile and has such duties as strapping a patient's feet to the table. She admitted that gangrene may result if the circulation of blood is cut off for more than fifteen or twenty minutes and further admitted that such result might follow from the use of these footstraps if they were tight enough. She maintained, however, that she did not believe that these straps could be made that tight. She then produced the straps in question and demonstrated to the jury how they are fastened to the feet by fastening them to the feet of one of the plantiff's physicians. This physician testified before the jury, after Miss Francis had fastened the strap to one of his feet, and he demonstrated that the strap tightens from the weight of the foot and leg, and would continue to tighten from such weight. It is significant to note, said the court, that these straps bind the feet at the very place where the plaintiff's gangrenous sores appeared.

The hospital contended that the plaintiff's injuries were caused by the negligence of her privately employed nurse in placing too hot a water bottle to her feet, but, said the court, there is absolutely nothing in the record to justify such a contention. The evidence showed conclusively that the water bottle was applied to the bottom of the feet and not to the outside. It is inconceivable that a hot water bottle could have been placed in such a manner as to blister one place on the outside of each foot, both in identically the same location, without also blistering some other part. The demonstration made before the jury, coupled with the testimony of the plaintiff's physician, was such that the jury could have found, as reasonable men, that the straps continued to tighten on the plaintiff's feet to the extent of obstructing the circulation of blood therein, that reasonable care on the part of the defendant required a temporary loosening of these straps and that a failure so to do proximately caused the injuries to the plaintiff. In fact, concluded the Supreme Court, the evidence excluded every causal connection except the straps, and we are of the opinion that the lower court erred in refusing to submit the case to the jury.

The doctrine of res ipsa loquitur does not in any instance create a case of absolute liability but simply raises a presumption or makes out a prima facia case of negligence to the extent that the defendant is called on to meet it with an explanation. Aside from the stated doctrine, and without applying the familiar Latin phrase thereto, the same result is effected under the general rules applying to circumstantial evidence. The case presented by the record here, said the court, rises above the domain of mere conjecture or possibility and presents facts and circumstances from which a jury might reasonably find that the defendant was guilty of negligence proximately contributing to the plaintiff's injury. It matters not, continued the court, whether our decision be grounded on the doctrine of res ipsa loquitur as interpreted by some of the courts and textbook writers or whether it be that the case here presented is based on circumstantial evidence from which a reasonable inference or presumption of negligence may be drawn, we are nevertheless of the opinion that the plaintiff's case should have been submitted to a jury for decision and that consequently the direction of a verdict against her was erroneous. The judgment of the trial court in favor of the hospital was accordingly reversed and the cause remanded for a new trial. *Palmer v. Clarsdale Hospital, 40 S. (2d) 582 (Miss., 1949).*

Evidence: Admissibility of Results of Lie Detector Tests.—The defendant was convicted of uttering and publishing forged checks and from such conviction appealed to the Supreme Court of Nebraska.

Evidence for the state consisted mainly of testimony tending to identify the defendant as the woman who uttered and published checks proved to have been ficticious. The defense consisted of testimony tending to establish an alibi and evidence tending to prove that the handwriting on the checks was not that of the defendant. In addition, the defendant called a witness who testified that he was a polygraph operator for the Nebraska Safety Patrol. He testified that a polygraph machine, commonly referred to as a lie detector, makes recordings of the increase and decrease of blood pressure, the increase and decrease of perspiration, and the inhalation and expiration of breath. He described the machine and the manner in which it makes the recordings and testified that the defendant voluntarily submitted to certain tests. The defendant then offered the witness to testify to and prove the results of the tests so made, which, the defendant contended, would show a normal reaction to all questions propounded with reference to the commission of the offenses charged and thus would indicate that the defendant was not guilty of such offenses. The state's objection to the admission of such testimony was sustained by the trial court.

In approving the action of the trial judge in refusing to admit in evidence the results of such tests, the Supreme Court said that it is apparent from reported cases of other jurisdictions that the scientific principle involved in the use of such polygraph has not yet gone beyond the experimental, and reached the demonstrable, stage and that it has not yet received general scientific acceptance. Experimenting psychologists themselves, the court said, admit that a wholly accurate test is yet to be perfected. Cogent reasons to support the general rule against the admission of such evidence readily suggest themselves, continued the Supreme Court, and if such evidence were admitted the vital function of cross examination would be impaired and the untrained jury would be charged with the task of evaluating psychologic factors not weighed or measured by the machine and understood only by trained operators.

The court concluded, therefore, that the trial court did not err in rejecting this evidence. The conviction, however, was

set aside on other grounds and the case remanded for a new trial.

[In a specially concurring opinion three of the seven judges stated that on a retrial the results of the lie detector test made on the defendant, in the circumstances in this case, should be admitted in evidence if it were established that the operator was an expert in that field and that the apparatus used and the tests made thereunder had been given general scientific recognition as having efficacy. "That complicated and difficult questions may arise therefrom in the trial of cases should be no reason for the exclusion of such evidence. Modern court procedure must embrace recognized modern conditions of mechanics, psychology, sociology, medicine, or other sciences, philosophy, and history. The failure to do so will only serve to question the ability of courts to efficiently administer justice."] —*Boeche v. State, 37 N. W. (2d) 503 (Nebraska, 1949).*

Medical Motion Pictures

FILM REVIEWS

Kidney Function in Health and Kidney Function in Disease. Prepared in 1948 by Arthur C. Corcoran, M.D.; Don C. Hines, M.D., and Irvine H. Page, M.D. Produced by Mervin La Rue, Chicago. Sponsored by Lilly Laboratory for Clinical Research and procurable on loan from Medical Department, Eli Lilly and Company, Indianapolis 6.

KIDNEY FUNCTION IN HEALTH. 16 mm., color, sound, 1,386 feet, showing time thirty-eight minutes.

This film briefly describes the physiologic role of the kidneys, the principles of their function and, in detail, the activities of the nephron. After a description of blood flow through the glomerulus and the regulating mechanisms, the process of glomerular filtration is illustrated and discussed with respect to (1) the governing factors, (2) several renal function tests concerned with filtration, and (3) tubular function tests concerned with filtration. Tubular function is then illustrated by following the filtrate step by step through the tubules. The activities of the several sections of the tubule in altering the composition of the glomerular filtrate are made clear.

The film is unique and can be regarded as epoch making in educational medical pictures, since it does not attempt to teach the subject without the aid of accompanying lectures and laboratory experiments. Its objective is accomplished well; the film is a valuable adjunct to a course in physiology at the medical school level.

Renal function is too complex to be understood in one casual viewing. Each of the three parts of the film should be seen at least twice, with adequate discussion or lectures interposed between the showing of each part.

The film has its greatest value for second year students in medicine or at a time when the physiology of the kidney is discussed in the preclinical course in physiology. However, it has a definite value for advanced students in medicine, such as those taking courses in internal medicine in the clinical years, or for postgraduate students of medicine as refresher material. It also has a distinct advantage as an introduction to the companion film "Kidney Function in Disease." In this combination the film is valuable for showing to county or state medical society meetings or other groups at this level.

KIDNEY FUNCTION IN DISEASE. 16 mm., color, sound, 1,672 feet, showing time forty-six minutes.

The first part of this film illustrates primarily the renal mechanism as one etiologic factor in hypertension. The effects of hypertension in the production of obliteration and sclerosis are contrasted with the process of proliferative interstitial fibrosis and tubular obstruction. The pathophysiology of acute, subacute and chronic glomerulonephritis is presented. The role of sodium retention and of hypoproteinemia in the formation of edema is illustrated. The syndrome of lower nephron nephrosis is presented with respect to both pathophysiology and therapy. A comparison is made of essential hypertension, glomerulonephritis and pyelonephritis with respect to differences in physiologic disturbances and clinical manifestations. The last part of this film is devoted for the most part to uremia and aberrations in acid-base balance in renal failure. Factors involved in prerenal azotemia and the treatment of electrolyte deficiency are illustrated. Finally, the therapy of essential hypertension is summarized effectively.

The three parts of the film depict practically the entire mechanism of renal disease in forty-five minutes. An enormous amount of factual material is most accurately and clearly presented. This is done for the greater part by the use of animated drawings. However, the film still attempts to cover too much ground in the allotted time. The narration is often too fast for proper mental perception, and the scenes change too rapidly for satisfactory visual appreciation.

Aside from the excessive speed, the pathophysiology of renal diseases is admirably presented in an exhaustive, concise and authoritative manner rarely attained in films on similar subjects. Except for the rather fast pace of this picture, the photography, animation and narration are excellent.

A 42 page booklet supplements these two motion pictures. It is beautifully illustrated with 45 color drawings of key scenes from the films. It also contains the narration, edited to be read instead of heard, and a relatively brief bibliography, with particular emphasis on original contributions for recent developments and comprehensive reviews for more settled phases.

Renal function is too complex a subject to be comprehended in detail at one sitting. Therefore, it is recommended that the films be seen several times, with study and discussion between showings. The booklet may be used as a focal point in such study and discussion, as an index to more extended reading and as a source of later review of the subject.

Shades of Gray (PMF 5047). 16 mm., black and white, sound (2 reels), showing time sixty-four minutes. Prepared in 1948 by and produced by the United States Army. Procurable on loan from the Army Surgeon of the Army area in which the request originates.

This motion picture begins with a series of strikingly accurate presentations of the various mental disorders which soldiers may experience during training and combat. The cases illustrate a range from mild anxiety states, obsessive-compulsive neuroses and "psychosomatic" disorders to severe depressive reactions and paranoid psychoses. In each instance the life patterns of the affected soldier are traced to his early familial and environmental settings and the sensitivities therein developed are skilfully correlated with the circumstances that precipitate his final breakdown. At this juncture the film makes the important point that in terms of "mental health" no one is either "white or black"; instead, every person is a "shade of gray" which corresponds to a complex summation of his capacities to adapt to a combination of stresses for which he is inadequately equipped or prepared. Other sections of the film present the procedures employed in psychologic selective service examination and allocation, the inculcation of group morale during training and combat and the organizational setup employed by the Army for the evacuation and treatment of neuropsychiatric casualties. Perhaps the best sequences are those on dynamic methods of military psychotherapy: interviews, emotional catharsis, narcoanalysis, hypnotic suggestion, group therapy and various other technics of physical, emotional and social rehabilitation designed to return the soldier to military service or to a satisfactory civilian readjustment.

Despite the optimism of the closing scenes, the film also brings home to the most hardened observer the incalculable cost in sheer human misery that modern war exacts even from those who survive it.

This film is highly recommended for medical and psychiatric teaching and to intelligent lay and military groups interested in what psychiatrists learned in the last war and what may be in store in a future war.

The film is uniformly excellent in photography, sound recording, direction and content.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

18:269-296 (April) 1949

Pulmonary Cripples. W. H. Blank.—p. 269.
Hydatidiform Mole and Associated Chorionic Lesions. T. M. Boulware, C. D. Howe and W. C. Friday.—p. 272.
Tick Paralysis: Discussion and Case Report. L. M. Bashinsky and S. C. Little.—p. 276.

American Heart Journal, St. Louis

37:481-688 (April) 1949

Possibility of Constructing an Einthoven Triangle for a Given Subject. F. N. Wilson, J. M. Bryant and F. D. Johnston.—p. 493.
*Surgical Treatment of Hypertensive Heart Disease and of Heart Failure of Hypertension. I. Chávez and L. Méndez.—p. 523.
*Coronary Vasodilator Action of Khellin. G. V. Anrep, M. R. Kenawy and G. S. Barsoum.—p. 531.
Further Studies of Circulation with Radioactive Erythrocytes. G. Nylin and S. Hedlund.—p. 543.
Complete Transposition of Aorta and Levoposition of Pulmonary Artery: Clinical, Physiologic and Pathologic Findings. H. B. Taussig and R. J. Bing.—p. 551.
Studies on Coronary Circulation: IV. Effect of Shock on Heart and Its Treatment. E. Corday, H. C. Bergman, Lois L. Schwartz and others.—p. 560.
Electrocardiographic Diagnosis of Disturbances of Heart's Venous Circulation. L. Unghváry.—p. 582.
Graphic Registration of Basal Diastolic Murmurs. B. G. Wells, M. B. Ranpaport and H. B. Sprague.—p. 586.
Effects on Circulation of Smoking Cigarettes with Varying Nicotine Content. J. A. L. Mathers, M. C. Patterson and R. L. Levy.—p. 612.

Surgical Treatment in Hypertensive Heart Disease.—Chávez and Méndez point out that in the treatment of arterial hypertension by sympathetic denervation it has been assumed that hypertensive heart disease and especially heart failure contraindicated operative procedures. Patients with these handicaps are precisely the ones who most urgently need lowering of their blood pressure. At the Instituto Nacional de Cardiologia of Mexico operations have been performed on a number of hypertensive cardiac patients, all of whom were in heart failure, which in some was of extreme degree. Of the 11 patients operated on, 1 died from cerebral hemorrhage eleven days after operation; another succumbed the day after the operation from occlusion of the aqueduct of Sylvius, the result of an overlooked old meningitis; a third patient died in uremia ten months after operation. The other 8 patients improved and were still alive after one and one-half to three years and had shown no evidence of heart failure. Some of them had resumed normal life. Instead of being a contraindication, hypertensive heart disease is fundamentally an indication for surgical treatment as the only means of staying myocardial damage. Heart failure, when it is not accompanied by advanced lesions, may sometimes be corrected through the operative procedure, even in protracted cases in which digitalis and ouabain have failed.

Coronary Vasodilator Action of Khellin (Visammin).—Anrep and associates compare action of visammin (khellin, dimethoxy-methyl-furano chromone) with aminophylline on the coronary circulation and on smooth muscle of guinea pigs, on the heart-lung preparation and on the isolated rabbit heart. Khellin was clinically tried in 300 patients with coronary artery disease. The experimental observations show that khellin is a potent coronary vasodilator. Khellin has a prolonged action and remains in the circulation for many hours. Its action in dilating the coronary arteries was found to be at least four times stronger than that of aminophylline. Khellin can be used continuously in the treatment of angina pectoris and also for the relief of individual attacks of pain. It can be administered orally in doses of 50 to 100 mg. three times per day or as an intramuscular injection in doses of 100 to 200 mg. The drug produces a few side effects but is not toxic even after prolonged administration. It does not change the bleeding or coagulation time. Of 250 patients with angina pectoris treated with khellin, distinct improvement was noted in 140, moderate improvement in 85 and no effect in 25. The drug was given to 50 patients with recent coronary thrombosis to improve the collateral circulation and relieve associated anginal symptoms. The latter, at least, seemed to have been accomplished.

American Journal of Diseases of Children, Chicago

76:127-226 (Aug.) 1948

*Ovarian Tumors in Infants and in Children. M. E. Costin Jr. and R. L. J. Kennedy.—p. 127.
Use of Supplemented Milk for Infant Feeding. A. J. Vignec, Helen McNamara and H. L. Barnett.—p. 154.
Inhalation Therapy in Pediatrics. E. W. Black and H. G. Poncher.—p. 169.
Mother-Child ABO Incompatibility: Relation of Secretor Status to Mental Deficiency. H. Yannet and Rose Lieberman.—p. 176.
Vitamin A, Carotene and Ascorbic Acid Content of Nursery School Lunches. Virginia Lee Tompkins and Florence I. Scoular.—p. 184.
Possible Dissemination of Poliomyelitis Virus by Carriers. L. P. Gebhardt and J. D. Woodie.—p. 192.
Mechanism of Hyperbilirubinemia in Newborn Infant: Experimental Demonstration of Functional Hepatic Immaturity. Gladys J. Fashena.—p. 196.
Unilateral Multicystic Kidney in Infancy. W. E. Goodyear and D. E. Beard.—p. 203.
*Pseudohermaphroditism in Twins: Report of Tenth Case. T. W. Collier.—p. 208.

Ovarian Tumors in Children.—Costin and Kennedy report 22 cases of ovarian tumor in infants and children 14 years of age or younger in whom surgical treatment had been carried out at the Mayo Clinic during the past twenty-eight years. More than 200 cases of ovarian tumor in infants and children have been reported in the literature. In approximately one third of these the tumors were simple multilocular cysts, in one fourth dermoid cysts and in more than one third carcinoma or sarcoma. In recent years the diagnosis of sarcoma and carcinoma of the ovary in children has become much less frequent. Many of the tumors which were reported as sarcomas or carcinomas in the older literature were probably granulosa cell tumors or dysgerminomas. Simple cysts are relatively common ovarian tumors in infants and children. In this series of 22 cases, 7 were of simple cysts. Pain in the abdomen is the outstanding symptom, and torsion of the pedicle is a frequent complication. The latter occurred in 5 of the 7 cases. Simple cysts with a twisted pedicle are frequently confused clinically with appendicitis or appendical abscess. Cystadenoma of the ovary is rare in children. The 3 cases in this series were all in 14 year old children who had reached puberty. Cystadenocarcinoma of the ovary in children is correspondingly rare. Teratomas are the commonest ovarian tumor in children. In this series there were 10 cases. There were 7 cases of dermoid cysts and 3 of embryonic teratomas. The predominant symptoms are abdominal tumor and pain. Roentgenograms are useful in the preoperative diagnosis of dermoid cyst. The dermoid cyst type of teratoma is usually benign, but the embryonic type must be considered as potentially malignant. There was 1 case of dysgerminoma in this series. Dysgerminomas are unusual in that they are frequently associated with pseudohermaphroditism or genital hypoplasia. It is safest to consider them as malignant tumors and to treat them as such. There was 1 case of granulosa cell tumor; it is a rare cause of sexual precocity in children and must be considered in the differential diagnosis of this condition. The incidence of malignant granulosa cell tumor in children is low.

Pseudohermaphroditism in Twins.—The case of pseudohermaphroditism in twins described by Collier is the tenth such case recorded in the literature. The twins were born in March 1947, were living at the time this report was written and were classified as pseudohermaphrodites of the female external type. It is not possible to go beyond an anatomic study in infancy, but early diagnosis and plastic work is desirable. Surgical treatment should be done at preschool age or, certainly, in the prepubertal period. Observation of the structural development

and pregnandiol excretion may be supplemented by urethroscopic examinations, pneumoperitoneum and, if indicated, laparotomy, to determine the degree of sexual aberration present.

American Journal of Ophthalmology, Chicago

32:487-624 (April) 1949

New Approach to Some Problems of Retinal Vascular Disease. J. S. Friedenwald.—p. 487.
Use of Tantalum Implants for Inducing Permanent Hypotony in Rabbits' Eyes. M. U. Troncoso.—p. 499.
Investigation of Blood-Aqueous Barrier in Newborn: II. To Inulin. V. E. Kinsey and M. B. Williamson.—p. 509.
Harada's Disease. Mary G. Bruno and S. D. McPherson Jr.—p. 513.
Ocular Cysticercosis. L. Junior.—p. 523.
Apparent Rotation of Fixed Target Associated with Linear Acceleration in Flight. B. Clark and A. Graybiel.—p. 549.
Spastic Entropion Correction: Wheeler's Orbicularis Advancement. M. P. Motto and R. L. Alexander.—p. 557.
Higher Refractional Anomalies: Their Frequency in Different Groups and Countries. E. Schmerl.—p. 561.
Ocular Myasthenia Gravis: Report of 2 Cases. J. V. Lisman.—p. 565.

American Journal of Public Health, New York

39:433-576 (April) 1949. **Partial Index**

*Some Public Health Problems in Nuclear Fission Operations. A. E. Gorman and A. Wolman.—p. 443.
Housing and Health: Sanitary Aspects of the Dwelling. M. A. Pond. —p. 454.
Id.: Appraisal of Substandard Housing. E. A. Tiboni.—p. 459.
Id.: Provision of Good Housing. Catherine Bauer.—p. 462.
Id.: Planned Community. F. J. Adams.—p. 467.
Q Fever: History and Present Status. R. E. Dyer.—p. 471.
Id.: Experimental Q Fever in Cattle. E. J. Bell, R. R. Parker and H. G. Stoenner.—p. 478.
Id.: Q Fever Survey in Southwest Texas. J. V. Irons, J. N. Murphy Jr., A. B. Rich and A. E. Hill.—p. 485.
Id.: Complement-Fixing Antibodies with C. Burnetii Antigens in Various Geographic Areas and Occupational Groups in the United States. E. Strauss and S. E. Sulkin.—p. 492.
Epidemiology of Accidents. J. E. Gordon.—p. 504.

Public Health Problems in Nuclear Fission.—Gorman and Wolman discuss problems of environmental and industrial sanitation which exist in the atomic energy industry, pointing out that the Atomic Energy Commission is striving to counteract the objectionable or hazardous conditions at and in the vicinity of the plants in which nuclear fission is carried out. A great deal of work has been carried out and is in progress for resolving the problem of protecting man and his environment against radioactivity. The authors mention meteorologic research to determine the most favorable atmospheric conditions under which to carry out operations, studies on surface and subsurface contamination of water supplies and research on waste disposal. The importance of training sanitary engineers in these problems is emphasized.

American Journal of Tropical Medicine, Baltimore

29:173-268 (March) 1949. **Partial Index**

Mel B in Treatment of Human Trypanosomiasis. E. A. H. Friedheim. —p. 173.
Active Form of Tryparsamide, TPB, in Treatment of Human Trypanosomiasis. E. A. H. Friedheim.—p. 181.
*Five Day Peroral Treatment of Yaws with STB, New Trivalent Arsenical. E. A. H. Friedheim.—p. 185.
Viability of E. Histolytica Cysts in Soil. P. C. Beaver and G. Deschamps.—p. 189.
Effect of Acetic Acid on Viability of Endamoeba Histolytica Cysts. P. C. Beaver and G. Deschamps.—p. 193.
Note on Apparent Antagonism of Bacterial Intoxication to Plasmodial Infection. M. F. Boyd and F. D. Coelho.—p. 199.
Southwest Pacific Vivax Malaria: Clinical Features and Observations Concerning Duration of Clinical Activity. E. Hill and D. S. Amatuzio. —p. 203.
Potential Vectors of Japanese Encephalitis in Caroline Islands. H. S. Hurlbut and J. I. Thomas.—p. 215.
Report on Presence of Japanese B Encephalitis Neutralizing Antibody Among Filipinos and Certain Philippine Animals. E. S. Salafranca and L. Espiritu.—p. 219.
Preparation and Testing of Specific Antigen for Diagnosis of Human Strongyloidiasis. Mary Jane Crump Brannon and E. C. Faust. —p. 229.
Action of Some Alkylhydroxybenzenes on Pig Ascaris In Vitro. W. J. Williams, V. Schelling and F. W. Hartman.—p. 241.

Five Day Peroral Treatment of Yaws.—Friedheim points out that the treatment of yaws in individual cases does not present a problem, since penicillin, arsenicals and any one of the numerous bismuth preparations may achieve a cure. Problems arise in connection with mass treatment in the tropics, particularly in the West African bush, where the incidence of yaws reaches 75 per cent and hundreds of thousands of persons with yaws are scattered over huge territories. Peroral application seems the optimum method for mass treatment under the aforementioned conditions. A relatively nontoxic and stable form of 4-oxy-3-acetylaminophenylarsenoxide, i.e., the trivalent derivative of acetarsone, "STB," approaches closely the characteristics desirable for mass treatment in undeveloped territories. Clinical tests have been carried out in the mountainous forest regions of French Guinea. Eighty-eight subjects presenting definite classic yaws lesions, in 73 of the infectious and 15 of the noninfectious type, were chosen for the study. The cases of infectious disease included those with primary and secondary lesions. The treatment consisted of a single oral daily dose of 0.01 to 0.02 Gm. per kilogram of body weight on five consecutive days. Control examinations were made three months after treatment. The treatment brought about cicatrization in all 73 cases of infectious yaws and in 14 out of 15 cases of "crab yaws." No untoward effects occurred. The five day oral treatment of yaws seems to be appropriate for mass treatment in tropical countries.

Annals of Allergy, Minneapolis

7:155-300 (March-April) 1949. **Partial Index**

Treatment of Headache, with Particular Reference to Use of Cafergone (Ergotamine Tartrate and Caffeine) for Relief of Attacks. F. K. Hansel.—p. 155.
Immediate Urticarial Reactions to Intradermal Injections of Bacterial Antigens: Preliminary Report. B. Kraft, M. H. Mothersill and R. H. Nestmann.—p. 162.
*Immunity to Diphtheria Induced by Booster Dose of Alcohol-Refined, Alum-Precipitated Toxoids: Based on Study of Fifty-Nine Allergic Children. H. G. Rapaport and M. M. Peshkin.—p. 165.
Improved Tissue Culture Technic Adaptable to Clinical Testing for Bacterial Hypersensitivity of Tuberculin Type. H. Blatt, F. A. Nantz and Jeanne M. Rehm.—p. 170.
Origin of Patterns of Allergic Sensitization. R. P. Wodehouse.—p. 172.
Experimental Study of Effect of Alcohol and Alcoholic Beverages on Allergic Reactions. Susan C. Dees.—p. 185.
Role of Allergy in Rheumatoid Arthritis and Suggested Treatment: Preliminary Report. G. E. Rockwell.—p. 195.
Therapeutic Effects of Certain Antihistamine Drugs in Allergic Conditions: Comparative Study. H. L. Harris.—p. 206.
Spontaneous Rib Fracture in Bronchial Asthma. M. L. Gelfand.—p. 217.
Studies of Drug Sensitivity. O. C. Hansen-Pruss.—p. 219.
*Oral Pollen Absorption: Demonstrated by Controlled Passive Transfer Tests. T. M. Feinblatt and R. Love.—p. 228.
Nature of Benadryl Activity and Its Clinical Applications. T. H. McGavack.—p. 232.
Role of Streptococci in Bronchial Asthma: Etiologic Significance and Treatment with Streptococcus Filtrates. H. A. Heise.—p. 240.
Effect of Substitution of Antistine (Phenyl-Benzyl-Amino-Methyl-Imidazoline) for Benadryl or Pyribenzamine During Height of Ragweed Pollen Season. B. Dickstein.—p. 250.
Benadryl: Intravenous Use in Allergy. B. Zolov.—p. 254.
Allergy as Cause of Mulberry Hypertrophy of Inferior Turbinate. L. J. Wallner.—p. 258.

Immunity to Diphtheria.—Rapaport and Peshkin treated 59 allergic children, whose average age was 13, by injection of a booster dose of 0.5 cc. of alcohol-refined, alum-precipitated toxoids. In 34 of these combined diphtheria and tetanus toxoids were used and in 25 diphtherial toxoid alone. All of these children had been primarily immunized against diphtheria in early childhood, and the majority of them subsequently received one or more doses of the commonly employed diphtherial toxoids. Pillemer's new method of alcohol refinement and purification practically eliminated the allergenic fractions from the toxoids without disturbing its high antigenic potency. One week to four months after the booster injection had been given, the blood was tested in the 59 children one or more times, and the diphtherial antitoxin titer revealed that this new refined toxoid caused a rise in antitoxin as high as 128 units or more per cubic centimeter of blood. The rise in titer occurred in all the children and was 4 to 640 times, or an average of 123 times, above the corresponding antitoxin level obtained prior to the booster injection of toxoid. The maximum antitoxin titer ranged from 0.1 unit to 128 units per cubic centimeter of blood, and in the majority of patients occurred two months after the booster dose had been given. Neglible local reactions occurred at the site of the injection in 5 children. No child experienced an elevation of temperature or an allergic reaction after the booster injection of alcohol-refined, alum-precipitated toxoid. The alcohol-refined, alum-precipitated diphtherial toxoid, alone or com-

bined with tetanus toxoid, can be currently regarded as the most ideal and reliable preparation for immunization against diphtheria.

Oral Pollen Absorption.—Feinblatt and Love injected serums from ragweed-sensitive donors and from summer-grasses-sensitive donors intracutaneously into the right and left arms, respectively, of 52 persons, 40 women and 12 men between the ages of 17 and 72 who were not sensitive to ragweeds or lawn grasses and therefore were selected as passive transfer subjects. They were divided into two groups; twenty-four hours after injection of the donor serum one group received 3 capsules of processed mixed ragweed, lawn grasses and common pollens (30 mg. in each capsule—a total of 90 mg. on a fasting stomach by mouth); the other group received 1,000 pollen units of commercially produced antigen by parenteral route. Twenty-five of the 52 persons had positive passive transfer reactions either to subcutaneous injections of 1,000 pollen units or to oral ingestion of 3 processed pollen tablets or both. Of the 25 who showed positive transfer reactions, 21 showed passive transfer reactions following the ingestion of the processed oral pollen antigen. The average time required for the development of the greatest response was 2.6 hours. Following injection of the commercially produced antigen, 20 of these persons showed positive transfer reaction. Development of the greatest reaction required an average of 2.6 hours. Control passive transfer tests thus demonstrated effective absorption by mouth of processed pollen antigens. Results suggest that the antigen response depends on a mechanism which is independent of the route of introduction of the antigen.

Archives of Dermatology and Syphilology, Chicago

59:127-250 (Feb.) 1949

Cutaneous Manifestations of Some Tropical Diseases. H. Fox.—p. 127.
Eczematous and Pustular Eruptions of Hands. M. H. Samitz.—p. 145.
Necrobiosis Lipoidica (Diabeticorum?): Histologic Study and Comparison with Granuloma Annulare. C. W. Laymon and I. Fisher.—p. 150.
Large Spores (Macroconidia, Fuseaux) of Microsporum Canis in Vivo: Report of 2 Cases. B. Appel and H. B. Ansell.—p. 168.
Human Infestation with Scabies of Monkeys. L. Goldman and M. D. Feldman.—p. 175.
Keratosis (Seborrheic and Senile). W. Sachs, G. M. MacKee and P. M. Sachs.—p. 179.
Pityriasis Versicolor: Atypical Clinical and Mycologic Variations. F. E. Bumgarner and Ruth C. Burke.—p. 192.
Dermatomyositis: Report of 3 Cases with Postmortem Observations. C. K. Wainger and W. F. Lever.—p. 196.
Inflammatory Ringworm Due to Trichophyton Faviforme: Report of 17 Cases. R. G. Carney.—p. 209.
Reiter's Syndrome with Keratotic Dermatitis: Report of Case. J. H. Peters.—p. 217.
Unusual Reactions to Intravenous Injections of Typhoid Vaccine. E. W. Thomas, M. Schur and M. Tye.—p. 230.

Archives of Internal Medicine, Chicago

83:1-118 (Jan.) 1949

Pathogenesis of So-Called Diffuse Vascular or Collagen Disease. K. Yardumian and J. Kleinerman.—p. 1.
Reaction of Body to Poliomyelitis and Recovery Process. A. C. Guyton.—p. 27.
Effects of Salicylates and Benadryl on Experimental Anaphylactic Hypersensitive Vascular and Cardiac Lesions. R. C. Roberts, K. A. Crockett and T. C. Laipply.—p. 48.
Hemosiderosis in Refractory Anemia. J. P. Wyatt and H. Goldenberg.—p. 67.
Syphilis: Review of Recent Literature. H. A. Tucker, C. F. Mohr, R. D. Hahn and J. E. Moore.—p. 77.

Archives of Ophthalmology, Chicago

41:125-252 (Feb.) 1949

*Role of Inheritance on Glaucoma. A. Posner and A. Schlossman.—p. 125.
Experimental Studies of Inclusion Blennorrhea: Isolation of Virus. A. E. Braley.—p. 151.
Use of Phenylephrine Hydrochloride (Neo-Synephrine Hydrochloride®) in Ophthalmology. P. Heath and C. W. Geiter.—p. 172.
Juxtapapillary Hemangioendothelioma of Retina: Report of Case. B. F. Souders.—p. 178.
Scleromalacia Perforans: Report of Case. M. Harbater.—p. 183.
*Congenital Ptosis: Classification of 200 Cases. R. N. Berke.—p. 188.
Intraorbital Tumors. A. W. Forrest.—p. 198.

Role of Inheritance in Glaucoma.—In the course of a study of 373 cases of primary glaucoma, Posner and Schlossman were impressed by the high incidence of the disease in patients displaying familial tendencies. Fifty-one patients had one or more relatives affected with the disease. A new approach is needed to the study of the role of inheritance in glaucoma, especially in the light of more recent advances in genetics. While this paper represents a limited experience, pooling of similar studies will supply enough data for a more adequate investigation of this genetic problem. Correlations made in the preparation of this survey suggested the possibility of using the hereditary group as a starting point for the investigation of some of the more elusive problems in glaucoma, such as (1) the preglaucomatous state, (2) the possibility of predicting the probable severity of the disease and (3) the relation between glaucoma and certain constitutional diseases. The 51 patients belonged to 30 different families. The authors present brief histories of these families and discuss the mechanisms of heredity. They found that in most families the disease follows a similar course in the various affected members. All the pedigrees show dominant heredity, except for 1, in which it may be recessive. Some sporadic cases may, on careful analysis, prove to be hereditary. The genetic approach may be an aid in the early recognition of glaucoma and in the study of the preclinical and mild phases of the disease.

Congenital Ptosis.—The classification of ptosis by Berke is based on a personal survey of the hospital records of 200 consecutive cases observed at the Institute of Ophthalmology, Presbyterian Hospital of New York City, during the past fifteen years. Normal superior rectus muscles were observed in 147 of the 200 cases, weakness of the homolateral superior rectus alone or combined with weakness of the homolateral inferior oblique in 34, the jaw-winking phenomenon of Marcus Gunn in 12 and ptosis associated with blepharophimosis in 7. Of the 200 cases the ptosis was unilateral in 145 and bilateral in 55, simple in 147 and complicated by horizontal or vertical anomalies in 53. In 107 of the 200 cases, sufficient action of the levator muscle existed to justify resection of the muscle as the operation of choice, while in 93 cases there was no such function and the patients were candidates for some modification of the Motais-Parinaud operation or for the frontalis type of procedure. This classification of congenital ptosis is useful, in that it shows the complicated nature of ptosis and, at the same time, is helpful in selecting the proper surgical procedure. It also gives the surgeon some idea of what to expect cosmetically and functionally from operations for the various types of congenital ptosis. In the hands of experienced surgeons inadequate cosmetic and functional correction of ptosis depends on the inherent complicated nature of the ptosis rather than on faulty judgment or technic.

Archives of Otolaryngology, Chicago

48:263-378 (Sept.) 1948

Stapes, Fissula Ante Fenestram and Associated Structures in Man: V. From Fetus of 160 Mm. (Five Months) to Newborn Infant. B. J. Anson and E. W. Cauldwell.—p. 263.
Benign Cysts of Superior Maxilla with Special Reference to Cysts of Maxillary Sinus: Clinicopathologic Study of 30 Cases. L. R. House.—p. 301.
Glycerite of Hydrogen Peroxide with Urea: III. Comparison by In Vitro Methods of Its Bacteriotoxic Action with That of Three Proprietary Aural Preparations. E. A. Brown, W. Krabek and Rita Skiffington.—p. 327.
Penicillin-Sulfanilamide Filling and Primary Suture in Simple Mastoidectomy. M. O. Abdeen.—p. 332.
Necrosis Within Pterygopalatine Fossa: Operation and Recovery. N. A. Fischer and A. J. Fischer.—p. 337.
Nasal Fractures: Analysis of One Hundred Cases. O. J. Becker.—p. 344.

Blood, New York

4:301-402 (April) 1949

Experimental Production of Nutritional Macrocytic Anemia in Swine. G. E. Cartwright, B. Tatting, H. Ashenbrucker and M. M. Wintrobe.—p. 301.
Use of Replacement Transfusion in Diseases Other Than Hemolytic Disease of Newborn. M. Bessis.—p. 324.
*Nitrogen Mustard Therapy in Hodgkin's Disease: Analysis of Fifty Consecutive Cases. W. Dameshek, L. Weisfuse and T. Stein.—p. 338.
Preparation of Stabilized Solutions of Hemoglobin. R. B. Pennell and W. E. Smith.—p. 380.
Effect of Cobalt on Oxygen Capacity and Methemoglobin Content of Blood. M. C. Bucciero and J. M. Orten.—p. 395.

Nitrogen Mustard in Hodgkin's Disease.—According to Dameshek and associates the most widely used nitrogen mustard is methyl bis (beta-chlorethyl) amine, subsequently abbreviated as HN_2. In tris (beta-chloroethyl) amine, or HN_3, the methyl

group is replaced by a third chloroethyl group. This report deals with the effects of nitrogen mustard in the authors' first 50 cases of Hodgkin's disease. They found it to be useful particularly in severe cases with constitutional symptoms and visceral involvement. In these cases a period of complete rehabilitation and a definite increase in life span of from two months to two years may follow the use of one or several courses of methyl bis (beta-chloroethyl) amine hydrochloride. This substance appears to have an almost specific affinity for the abnormal tissues of Hodgkin's disease. Its effects resemble closely those of roentgen radiation. It is often effective in producing complete remission in cases completely refractory to roentgen therapy. Radiosensitivity may return after a course of nitrogen mustard therapy. In involvement of the spinal cord or peripheral nerves, the compound is far more effective, particularly in pain relief, than is roentgen ray. Methyl bis (beta-chloroethyl) amine hydrochloride is likewise more effective in bringing about relief of fever and severe generalized itching than is roentgen radiation. Irradiation is the treatment of choice in relatively early cases of Hodgkin's disease, primarily because longer remissions can be obtained than with nitrogen mustard. The combined use of nitrogen mustard and roentgen rays may be the best treatment. Doses of methyl bis (beta-chloroethyl) amine hydrochloride somewhat smaller than the generally recommended 0.1 mg. per kilogram of body weight are usually effective and less likely to produce secondary effects such as granulocytopenia, which can usually be prevented by administration of penicillin. The only definite contraindication to the use of the nitrogen mustard is the presence of jaundice. Although cure of Hodgkin's disease cannot be expected, the remissions which are produced offer great comfort to the patient.

California Medicine, San Francisco

70:235-378 (April) 1949

*Use of Radioactive Iodine in Treatment of Graves' Disease. M. Prinzmetal, C. M. Agress, H. C. Bergman and B. Simkin.—p. 235.
Diagnosis of Intestinal Obstruction in the Newborn: Review of Literature with Report of Eight Additional Cases. E. Carlson, A. G. Clark and P. M. Walstad.—p. 240.
Hemolytic Anemias: Recent Advances in Diagnosis and Treatment. R. S. Evans and Rose Duane.—p. 244.
Median Nerve Injuries in Fractures in Region of the Wrist. N. Meadoff.—p. 252.
Rheumatoid (Marie-Strumpell) Spondylitis: Technic of Examination and Importance of Costal Joints. A. J. Williams.—p. 257.
Problems of General Practice in Rural California. H. L. Carey and C. B. Andrews.—p. 262.
Place and Training of the General Practitioner. W. Darley.—p. 265.
Spontaneous Pneumoperitoneum. W. L. Stilson and O. J. Neufeld.—p. 269.
Operation for Congenital Cataract. O. Barkan.—p. 274.
Pediatric Anesthesia. M. D. Leigh.—p. 278.
*End Results of Thoracolumbar Sympathectomy for Advanced Essential Hypertension. J. W. Hinton.—p. 282.
Otitis Externa. C. W. Rees.—p. 288.
Observations on Difficulties Encountered in Serological Diagnosis of Brucellosis and Q Fever. K. F. Meyer and B. Eddie.—p. 292.
Prescription for Light Work for Partially Disabled Employee. C. Leggo.—p. 294.
Cancer of Cervix. H. F. Traut.—p. 297.

Radioactive Iodine in Hyperthyroidism.—Prinzmetal and co-workers treated 50 patients with uncomplicated hyperthyroidism with radioactive iodine (I^{131}). Twenty-six patients were followed for one year or longer. Euthyroidism was restored in 25, and 1 patient was greatly improved. The total dose of radioiodine administered varied from 0.5 to 10 millicuries, averaging 4.4 millicuries. The average length of time required for return to a euthyroid state was three to four months. Hypometabolism developed in 3 patients, and 1 patient presented signs and symptoms of myxedema. No other complications ensued. One patient who apparently relapsed responded again after readministration of radioiodine. The uptake of I^{131} before treatment ranged from 31.7 to 100 per cent, with an average of 62.4 per cent, and after treatment ranged from 1.5 to 76.0 per cent, averaging 27.3 per cent. The determination of the uptake of radioiodine by the thyroid gland is a useful diagnostic procedure in the differentiation of conditions simulating hyperthyroidism. The thyroid gland decreased in size after treatment with radioactive iodine; the uptake of iodine by the gland was reduced, and the level of organic iodine in the plasma was restored to normal. In 4 cases of acute thyroiditis, in spite of a high basal metabolic rate, a high content of organic iodine in the plasma and other evidences of "hyperthyroidism" the uptake of I^{131} was very low. Radioactive iodine appears to be an effective therapeutic agent in the management of patients with thyrotoxicosis. It is not recommended for nodular goiters.

Thoracolumbar Sympathectomy.—Hinton performed thoracolumbar sympathectomy in 473 patients, 185 men and 288 women, 72 of them between the ages of 50 and 59, for essential hypertension during the six year period February 1942 to February 1948. Most of the patients had advanced stages of hypertensive disease. Patients were selected for operation on the basis of evaluation of the degree of damage in the brain, eye, kidney and heart. The total number of deaths in and out of the hospital in this period was 79, or a total mortality rate of 16 per cent. There were 38 in-hospital deaths, or a mortality rate of 8 per cent. The causes of death occurring in the hospital were, in order, as follows: cerebral accident, cardiac failure and renal insufficiency. The out-of-hospital deaths were, in order, as follows: cardiac failure, cerebral accident and renal insufficiency. Operations done early in the series in approximately 150 cases followed the Smithwick procedure including nine thoracic ganglions through the second lumbar ganglion with removal of the greater, lesser and least splanchnic nerves, but later the minimal operative procedure included the third thoracic ganglion through the third lumbar ganglion with all the splanchnic nerves. In addition, 40 total sympathectomies were performed which included the stellate ganglion. Results from the most extensive operation were better than those from the lesser procedure, but the mortality rate was also greater. Conclusion that complete or nearly complete sympathectomy is preferable to a less extensive procedure must await the collection of more data which can be used in weighing the respective end results against the mortality. Thoracolumbar sympathectomy has a definite place in the treatment of hypertensive vascular disease, but in advanced disease it is chiefly palliative.

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Acute Respiratory Infections: Contributions Made During World War II. J. H. Dingle.—p. 117.
Advances in Treatment of Diseases of Chest. A. L. Barach.—p. 131.
Fluid Therapy in Acute Illness of Infancy and Childhood. Katharine Dodd and S. Rapoport.—p. 135.

30:181-242 (April) 1949

Socio-Economic Problems Confronting Medicine. P. R. Hawley.—p. 181.
Therapeutic Use of Artificially Prepared Radioactive Isotopes. C. V. Moore.—p. 192.
Application of Respiratory Physiology in Treatment of Respiratory Diseases. R. T. Thompson.—p. 194.

Diseases of Chest, Chicago

15:377-506 (April) 1949

*Surgical Treatment of Mitral Stenosis (Mitral Commissurotomy). C. P. Bailey.—p. 377.
Importance of Continued Studies in Tuberculosis. H. L. Mantz.—p. 398.
Early Diagnosis as Means of Tuberculosis Control. E. D. Rames.—p. 404.
*Diagnosis of Cancer of Lung by Cytologic Method. G. N. Papanicolaou and H. A. Cromwell.—p. 412.
One-Half Gram of Streptomycin in Treatment of Pulmonary and Extrapulmonary Tuberculosis: Report of 120 Cases. R. W. Dickman.—p. 422.
Streptomycin in Tuberculosis of Larynx. B. Margulies.—p. 432.
Aerosol Antibiotic Therapy in Suppurative Diseases of Lung and Bronchi. B. P. Potter.—p. 436.
Bronchogenic Carcinoma. D. D. Feld and V. O'Malley.—p. 450.
Pathogenesis of Pulmonary Atelectasis. R. Viswanathan.—p. 460.
Lipoid Pneumonia in Neuropsychiatric and Debilitated Patients. A. A. Humphrey and E. G. Olmstead.—p. 471.
Mediastinal Tumors and Cysts. J. V. Thompson.—p. 480.

Surgical Treatment of Mitral Stenosis.—In mitral stenosis, which is usually due to rheumatic fever, the valve cusps become thickened, shortened and fibrotic. The cusps appear to fuse at the commissures, so that the opening becomes a slit in a thickened, fibrotic placque, through which regurgitation occurs. Localized involvement may obstruct two thirds of the normal valve opening and thus be responsible for the stenosis of an otherwise not too distorted valve. It occurred to Bailey to

cut such a placque completely in two by two incisions at the commissures of the valve opening, so that the two halves of the placque could separate freely, being hinged by soft valvular tissue at either extremity. He presents histories of patients who were subjected to the surgical treatment. One of these survived and showed a gratifying result. Another patient could have survived if the author had known then what he learned since. The disease in the third patient probably was too advanced for help. In 2 other patients surgical treatment was started but could not be completed. The author believes that the mitral valve is best approached through the left auricular appendage by an anterolateral approach. Accurate surgical maneuvers depend on control by vision or digital palpation. Commissurotomy should be limited to patients with single valve lesions without rheumatic activity. Commissurotomy seems preferable to a shunt operation (azygos-pulmonary vein anastomosis or opening of the interauricular septum). Preoperative digitalization, quinidinization and the intravenous use of procaine during intervention are valuable in supporting cardiac function and in preventing arrhythmia. Antibiotics are given to prevent infection. Recently 5 additional patients were operated on. Two of these were well at the time of reporting; 1 died two and a half months after operation; 1 died as the result of an error in technic at operation (cutting across a valve leaflet), and 1 was getting along well for six days but died suddenly of a cerebral arterial embolus.

Cytologic Method in Diagnosis of Cancer of Lung.—Papanicolaou and Cromwell say that the fixation and staining method in the study of sputum for cancer cells was first used by them in June 1945. Since that date 1,300 cases have been studied. The accuracy was approximately 95 per cent for the positive reports and 85 per cent for the negative results. The method helps in the diagnosis of cases of obscure disease. In some instances in which bronchoscopic examination and aspiration biopsy gave negative results and the results of roentgen examination were inconclusive, a positive sputum revealed the true nature of the lesion. The method aids in the earlier diagnosis of pulmonary neoplasm. It is of value for screening purposes in cancer detection clinics. It tends to accelerate the diagnosis and to increase the percentage of operable lesions. It is particularly useful in establishing a diagnosis of carcinoma of the superior sulcus, so-called Pancoast's tumor. Tumors in this part of the lung are inaccessible to the bronchoscope. When roentgen findings are meager, bronchial washings from both right and left main bronchi may decide the issue. Because of the technical simplicity and low cost of the method, repeated specimens can be obtained, making it particularly advantageous in postoperative and postirradiation follow-up.

Florida Medical Association Journal, Jacksonville

35:601-668 (April) 1949

Laryngofissure and Laryngectomy in Treatment of Intrinsic Carcinoma of Larynx. J. B. Farrior.—p. 619.
Type of Anesthesia in Herniorrhaphy with Reference to the Aged. J. L. Selden Jr.—p. 622.
Plan of Conservative Management of Antepartum Eclampsia. S. L. Watson Jr.—p. 626.
General Principles in Treatment of Tuberculosis. R. D. Thompson.—p. 630.
Progress in Public Health in Florida. W. T. Sowder.—p. 635.
Amebiasis and the Proctologist. R. F. Allen.—p. 640.

Indiana State Medical Assn. Journal, Indianapolis

42:185-300 (March) 1949

Role of Analgesia and Anesthesia in Production of Asphyxia Neonatorum. D. M. Little Jr. and R. M. Tovell.—p. 201.
Why Malaria Cures General Paralysis. W. L. Bruetsch.—p. 211.
Treatment of Supracondylar Fracture of Humerus. J. C. Donchess.—p. 217.
Electrocardiogram in Acute Pericarditis: Comparison of Cases With and Without Effusion into Pericardial Sac. R. M. Nay.—p. 222.

42:301-398 (April) 1949

Malignant Melanoma: Discussion of 65 Pathologically Proven Cases. N. D. Ewing.—p. 317.
Symptoms and Prompt Diagnosis of Tumors of Genito-Urinary Organs. A. L. Dean.—p. 321.
Rational Therapy of Carcinoma of Cervix. J. L. Loudermilk.—p. 327.
Problem of Carcinoma of Breast. R. R. Buchholz.—p. 332.
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Iowa State Medical Society Journal, Des Moines

39:100-138 (March) 1949

Chronic Intestinal Insufficiency (Celiac Disease) in Children. C. D. May.—p. 100.
Acute Diarrhea in Children. I. H. Borts.—p. 103.
Immunization Procedures Brought Up to Date. J. E. Dyson.—p. 105.
Bandl's Ring: Report of Case. D. C. Sharpe.—p. 107.
General Practitioner in This Era of Specialization. M. J. Carey.—p. 110.

39:139-186 (April) 1949

Electrocardiographic Changes Associated with Myocardial Infarction. L. E. January.—p. 142.
*Anticoagulants in Treatment of Acute Myocardial Infarction and Its Complications. W. B. Bean.—p. 149.
Congenital Malformations of Heart and Great Vessels: Diagnosis and Treatment. J. L. Ehrenhaft.—p. 153.

Anticoagulants in Myocardial Infarction.—Bean lists the considerations which form the basis of the use of anticoagulant compounds in the treatment of patients with acute myocardial infarction. Anticoagulant therapy has been shown to reduce the incidence and severity of thromboembolic accidents following in the wake of acute infarction of the heart. The mortality rate has been reduced significantly in controlled studies. Treatment should be instituted at the time the patient is first seen or within two weeks of the onset of acute myocardial infarction and continued four weeks after the attack. Anticoagulant treatment is dangerous and should never be used unless there is a daily check on blood prothrombin levels by competent laboratory personnel. The patient must be hospitalized. For early cases, dicumarol® alone is effective, but, since there is a one or two day delay in obtaining full effect, heparin may be used for its rapid effect. There is some risk of hemorrhage, even with meticulous laboratory control, but it is minor in comparison with the gains from prevention of thromboembolism. Anticoagulants are not contraindicated unless a hemorrhagic state exists. The conventional forms of therapy must not be suspended because of anticoagulant therapy.

Journal of Clin. Endocrinology, Springfield, Ill.

9:213-300 (March) 1949

Antihormone Formation Complicating Pituitary Gonadotropin Therapy in Infertile Men: I. Properties of Antihormones. W. O. Maddock.—p. 213.
Pregnandiol Precipitation Test: Further Observations on Clinical Applications and Technic. H. C. Mack, A. E. Parks and M. McDonald.—p. 234.
Carbohydrate Metabolism in Combination of Diabetes Mellitus and Addison's Disease, as Illustrated by Case. J. H. Crampton, S. T. Scudder and C. D. Davis.—p. 245.
Corticoadrenal Tumor with Hypoglycemic Syndrome, Goiter, Gynecomastia and Hepatosplenomegaly. J. J. Staffieri, O. Cames and J. M. Cid.—p. 255.
Urinary Excretion of Chorionic Gonadotropin by Human Females Following Parenteral Administration of Aqueous or Beeswax Solutions. C. W. Lloyd, E. C. Hughes, M. L. Eva and J. Lobotsky.—p. 268.
*Results of Prolonged Medical Treatment of Obesity with Diet Alone, Diet and Thyroid Preparations, and Diet and Amphetamine. D. Adlersberg and M. E. Mayer.—p. 275.
Utero-Tubal Persufflation Curve in Myxedema: Effect of Thyroid Therapy. J. C. Mussio Fournier and A. Pou de Santiago.—p. 285.

Treatment of Obesity.—Adlersberg and Mayer report treatment of obesity under controlled conditions in the nutrition clinic of a large general hospital during an observation period of five and one-half years. The study included 299 patients, 27 men and 272 women. Moderate uncomplicated hypertension without evidence of heart failure was present in about 25 per cent of the group. In group A, in which only low caloric diets were employed, the average weight loss increased in proportion with the degree of obesity. Diet alone resulted in better weight reduction than diet plus thyroid medication (group B), whereas diet plus amphetamine therapy (group C) showed somewhat better results than diet alone. Amphetamine sulfate reduced the appetite, but this effect often faded with continued administration of the drug, so that with the same dosage of amphetamine increased food intake and weight gain resulted. To avoid this, the dose of amphetamine had to be gradually raised. In some persons addiction to amphetamine developed. Two instances of amphetamine poisoning were observed in psychoneurotic patients who had refilled the prescription for amphetamine sulfate on many occasions and had raised the dose to toxic levels. Although no serious complications resulted in these cases, amphetamine may cause poisoning by accident or by uncritical

use. Regardless of the form of therapy employed, best results were obtained in the first two months of treatment. In the later stages of treatment amphetamine proved to be superior to thyroid. Long term results with diet alone compared favorably with those obtained with diet and amphetamine. Short term effects should be strictly separated from the long range results in studies on weight reduction, since the immediate success is usually much better than the ultimate result.

Journal of Clinical Investigation, Cincinnati

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Studies of Role of Liver in Human Carbohydrate Metabolism by Venous Catheter Technic: I. Normal Subjects Under Fasting Conditions and Following Injection of Glucose. P. K. Bondy, D. F. James and Betty W. Farrar.—p. 238.
*Metabolic Studies on Protein-Depleted Patients Receiving Large Part of Their Nitrogen Intake from Human Serum Albumin Administered Intravenously. Christine Waterhouse, S. H. Bassett and J. W. Holler. —p. 245.
Effects of Induced Malaria, Acute Starvation and Semi-Starvation on Electrophoretic Diagram of Serum Proteins of Normal Young Men. H. L. Taylor, O. Mickelsen and A. Keys.—p. 273.
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Hematologic Observations in Patients with Chronic Hepatic Insufficiency: Sternal Bone Marrow Morphology and Bone Marrow Plasmacytosis. T. Jarrold and R. W. Vilter.—p. 286.
Cardiovascular Effects of Acutely Induced Hypothermia. O. Prec, R. Rosenman, K. Braun and others.—p. 293.
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Clotting Behavior of Human "Platelet-Free" Plasma: Evidence for Existence of "Plasma Thromboplastin." C. L. Conley, R. C. Hartman and W. I. Morse II.—p. 340.
Hemodynamic Effects of Hypotensive Drugs in Man: I. Veratrum Viride. E. D. Freis, J. R. Stanton, J. W. Culbertson and others.—p. 353.
Observations on Ballistocardiographic Pattern, with Special Reference to H and K Waves. J. L. Nickerson.—p. 369.
Effect of Adrenocorticotrophic Hormone in Congenital Adrenal Hyperplasia with Virilism and in Cushing's Syndrome Treated with Methyl Testosterone. R. A. Lewis and L. Wilkins.—p. 394.

Human Serum Albumin in Protein-Depleted Patients.—Waterhouse and associates say that when purified human serum albumin became available in large quantities through the Red Cross program, it was observed to have certain advantages over other materials in common use for the correction of protein depletion. Each of 4 subjects was given a daily dose of 60 Gm. of concentrated sodium-free albumin for ten or more days. Balances of nitrogen, calcium, phosphorus and potassium were made during control, albumin and postalbumin periods. Concomitant observations of serum protein fractions, plasma volume and renal function were made. Each of the 4 patients reacted differently; the variations were as follows: (1) development of intense proteinuria in a patient convalescent from rheumatic fever, without evidence of impaired renal function; (2) retention of water with peripheral edema, hydrothorax and pericardial effusion and poor utilization of the injected protein in a woman with probable generalized vascular disease; (3) excellent utilization, but eventual development of signs of cardiorespiratory embarrassment in a young woman in fair health except for moderate undernutrition, and (4) modification of the response in a normal young man by other dietary factors. The clinical response to human serum albumin given intravenously depends not only on its nutritive properties as a protein but also on two other factors, its potent osmotic activity and its nativity to the human body. Probably because of the last-named factor it is metabolized comparatively slowly in normal circumstances. When the substance is given in large quantities, its slow utilization results in the accumulation of significant amounts of osmotically active protein. To predict the response of the patient to injections of human albumin, one should take into consideration (*a*) his state of nutrition, especially with respect to protein, (*b*) the permeability of the capillaries in general and of the glomerulus in particular and (*c*) the status of the cardiac reserve. Proteinuria will develop eventually in any patient when saturation with albumin has occurred, and this is probably not due to renal damage but represents a physiologic response when the maximum reabsorptive capacity of the renal tubules for protein is exceeded.

Journal of Gerontology, Springfield, Ill.

4:1-89 (Jan.) 1949

Biologic Approach to Aging Processes. J. C. Aub.—p. 1.
Senility and Intestinal Flora: Reexamination of Metchnikoff's Hypothesis. S. Orla-Jensen, E. Olsen and T. Geill.—p. 5.
Serum Silica Concentration at Various Ages. S. A. Kvorning and E. Kirk.—p. 16.
Some Factors Affecting Vocabulary Size in Later Maturity: Age, Education, and Length of Institutionalization. Charlotte Fox and J. E. Birren.—p. 19.
Intravenous Glucose Tolerance Tests in Aged Males. L. E. Smith and N. W. Shock.—p. 27.
Urinary Excretion of Neutral 17-Ketosteroids in Middle-Aged and Old Men. E. Kirk.—p. 34.
Cardiovascular Survey of Residents in Custodial Institution for the Aged. M. Dolgin, M. Grossman, A. J. Simon and others.—p. 39.
Teaching Geriatrics: Basic Principles and Syllabus of Course Now in Fifth Year. F. D. Zeman.—p. 48.

Journal of Immunology, Baltimore

61:119-208 (Feb.) 1949

Quantitative Studies in Anaphylaxis. III. Effect of Alum Adjuvant and Route of Administration on Sensitizing Dose. E. J. Coulson and H. Stevens.—p. 119.
More Accurate Method for Statistical Evaluation of Effects of Vaccination. E. Carlinfanti.—p. 125.
Immunological Evidence on Role of Lymphocyte in Antibody Formation. K. Habel, K. M. Endicott, J. F. Bell and Frances Spear.—p. 131.
Isolation of Serum Lipid Which Inhibits Serologic Reactions. E. Volkin.—p. 143.
Measurement and Preservation of Antibodies in Human Sera. M. Heidelberger and Marie M. Dilapi.—p. 153.
Flagellar Antigens of Escherichia Coli. C. A. Stuart and P. L. Carpenter.—p. 161.
Blood Groups and Subgroups of Newborn. I. The A Factor of Newborn. E. Witebsky and Lillian M. Engasser.—p. 171.
Antibody Response of Rabbits to Single Injection of Type I Pneumococci. C. M. MacLeod, M. Heidelberger, Betty Robinson and others.—p. 179.
Antihyaluronidase Content of Human Blood Serum: Study in Age Differences. R. W. Quinn.—p. 185.
Influenzal Antibodies in Lymphocytes of Rabbits Following Local Injection of Virus. Susanna Harris and T. N. Harris.—p. 193.

Journal of Neurophysiology, Springfield, Ill.

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Pattern of Tactile Representation in Thalamus of Cat. V. Mountcastle and E. Henneman.—p. 85.
Effect of Preoccipital and Temporal Decortication on Learned Visual Discrimination in Monkeys. H. W. Ades and D. H. Raab.—p. 101.
Irritability of Mammalian Nerve Following Ischemia. E. L. Porter and P. S. Wharton.—p. 109.
Study of Multiplied Cortical Response to Repetitive Stimulation in Thalamus. W. S. Fields, R. B. King and J. L. O'Leary.—p. 117.
Effect of Localized Cutaneous Stimulation on Circulation in Duodenal Arterioles and Capillary Beds. C. A. Richins and K. Brizzee.—p. 131.
Effects of Barbiturates and Ether on Spontaneous Electrical Activity of Dog Brain. R. L. Swank and C. W. Watson.—p. 137.

Journal of Neurosurgery, Springfield, Ill.

6:97-186 (March) 1949

Cervical and Lumbar Pilonidal Sinus Communicating with Intraspinal Dermoids: Report of 2 Cases and Review of Literature. E. Sachs Jr. and G. Horrax.—p. 97.
Technic for Transplant of Musculospiral Nerve in Open Reduction of Fractures of Mid-Shaft of Humerus. M. T. Schnitker.—p. 113.
Follow-up Report of Spinal Cord Injuries in Group of World War II Patients. R. C. Schneider, J. E. Webster and J. E. Lofstrom.—p. 118.
Subdural Empyema. W. S. Keith.—p. 127.
Physiological Salt Solutions for Brain Surgery: Studies of Local *p*H and Pial Vessel Reactions to Buffered and Unbuffered Isotonic Solutions. K. A. C. Elliott and H. H. Jasper.—p. 140.
Paraphysial Cysts of Third Ventricle with Report of 8 Cases. J. Greenwood Jr.—p. 153.
Results of Operations for Lumbar Protruded Intervertebral Disk. J. Raaf and G. Berglund.—p. 160.

Journal of Urology, Baltimore

61:473-670 (March) 1949. **Partial Index**

Importance of Accurate Pathologic Classification in Prognosis of Renal Tumors: Second Report. N. C. Foot, G. A. Humphreys and W. F. Whitmore Jr.—p. 477.
*Treatment and Prognosis of Papillary Tumors of Renal Pelvis and Ureter. V. J. O'Conor.—p. 488.
Tumors of Ureter. F. C. Hamm and L. L. Lavalle.—p. 493.
Cystic Ureterovesical Protrusion: Report of 4 Cases in Children and 2 in Adults. H. O. Mertz, J. W. Hendricks and R. A. Garrett.—p. 506.
Transplantation of Ureter in Intractable Vesical Tuberculosis. A. Jacobs. —p. 517.
Rhabdomyosarcoma of Urinary Bladder. H. J. Meisel, W. H. Heath and J. M. Miller.—p. 525.
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Vesico-Intestinal Fistulas: Report of 2 Cases of Fistula Between Bladder and Large Intestine Cured Without Preliminary Diversion of Fecal Stream. J. K. Ormond.—p. 554.
Female Urethra: Clinico-Pathologic Study. N. B. Powell and Elizabeth B. Powell.—p. 557.
Radical Surgery in Prostatic Carcinoma. F. P. Twinem and A. Davalos. —p. 575.
Carcinoma of Prostate: Statistical Study and Evaluation of Endocrine Therapy, with Preliminary Report on Additional Method of Treatment. H. Q. Gahagan and J. L. Fischman.—p. 587.
Anatomic Study of External Urethral Sphincter in Relation to Prostatic Surgery. H. C. Rolnick and F. K. Arnheim.—p. 591.
Radical Cure of Varicocele by New Technic: Preliminary Report. A. Palomo.—p. 604.
Anuria: Report of 27 Cases. J. K. Ormond and J. W. Best.—p. 608.
Manifestations of Lymphoblastomas in Genito-Urinary Tract. E. M. Watson, H. R. Sauer and M. G. Sadugo.—p. 626.
Application of Detergents to Urology. R. E. La Rue.—p. 646.
Clinical Study of New Sulfonamide (NU-445) in Treatment of Urinary Tract Infections. J. A. Lazarus and L. H. Schwarz.—p. 649.
Further Studies Relative to Treatment of Urinary Tuberculosis by Chemotherapy. G. E. Slotkin and W. Spencer.—p. 658.

Papillary Tumors of Renal Pelvis and Ureter.—O'Conor reports 482 nephrectomies and 16 renal explorations. An unusually high incidence of renal pelvic and ureteral tumors occurred in this series. Of patients who had nephrectomy for renal or ureteral tumor, 48 had cortical tumors while in 14 the tumor was primarily in the renal pelvis with secondary implants in ureter or bladder. Of these latter, 12 were papillary carcinomas and 2 were squamous cell tumors. There were 8 primary ureteral tumors, all papillary. Of the 12 papillary carcinomas primarily in the renal pelvis, 6 had implants in the ureter and in 4 small papillary tumors of the bladder were observed at the first examination. The treatment of choice for papillary tumors arising primarily in the renal pelvis or ureter is complete nephroureterectomy. Incomplete ureterectomy is often followed by recurrence, or subsequent tumor development in the ureteral stump, the intramural portion of ureter or the bladder mucosa. These secondary tumors are usually more extensive than the primary lesion and as a rule are less amenable to destruction. Papillary tumors of the upper part of the urinary tract are often associated with stone and chronic infection. Microscopic study of the ureters which have been removed from these patients suggests a widespread or diffuse metaplastic response to an apparent carcinogenic agent on the part of the ureteral epithelium. There is no justification in one's making a diagnosis of "benign" papillary tumor of the renal pelvis or ureter. To recommend local excision of ureteral tumors would seem a step backward in the treatment of the only neoplastic condition of the upper part of the urinary tract in which complete surgical treatment has improved the end results and period of postoperative survival.

Maine Medical Association Journal, Portland

40:59-75 (March) 1949

Anesthesia in Hypertensive Patient. G. Clapperton.—p. 59.
Urological Aspects of Hypertension. J. Memmelaar.—p. 61.
Cardiac Arrest with Recovery: Case Report. M. Ridlon, R. Feeley and C. S. Dwyer.—p. 62.
Surgical Aspects of Hypertension. G. L. Maltby.—p. 64.

40:75-98 (April) 1949

Colpectomy—in Management of Prolapse of Uterus and Vagina. L. A. Sweatt.—p. 75.
Fluorine and Its Effect on Teeth. H. I. Marcotte.—p. 77.
Tachycardia and Its Treatment. B. Beliveau.—p. 78.
Industrial Physician and Family Doctor. B. W. Russell.—p. 79.
Duodenal Ulcers: Some Surgical Aspects. A. F. DuMais.—p. 81.

Medicine, Baltimore

28:1-142 (Feb.) 1949

Pulmonary Insufficiency: II. Study of 39 Cases of Pulmonary Fibrosis. Eleanor deF. Baldwin, A. Cournand and D. W. Richards Jr.—p. 1.
*Pathology of Thymus in Myasthenia Gravis: Study of 35 Cases. B. Castleman and E. H. Norris.—p. 27.
Landry-Guillain-Barré Syndrome: Clinicopathologic Report of 50 Fatal Cases and Critique of Literature. W. Haymaker and J. W. Kernohan. —p. 59.

Thymus in Myasthenia Gravis.—Castleman and Norris discuss the pathologic findings in the thymus gland in 35 cases of myasthenia gravis. In 10 patients all or a portion of the thymus was replaced by a neoplasm; in the others, the thymus was grossly normal with respect to size and weight but on microscopic examination showed varying degrees of lymphoid germinal center infiltration of the medulla. Statistical data compiled from the 35 cases and from 297 cases collected from the literature demonstrated that the non-neoplastic thymus is more frequent in female subjects between the ages of 15 and 35 in contrast to the thymoma, which is more apt to develop in men between 40 and 60 years of age. Symptoms of myasthenia gravis are usually of shorter duration in the patient with thymoma. The thymic tumor of myasthenia gravis is usually an encapsulated, slowly growing, benign neoplasm, weighing about 70 Gm. In about 10 per cent of the cases it may encroach on neighboring structures and may produce local implants, but it has never been known to truly metastasize or to occur outside the thoracic cavity. The tumors are composed of both epithelial and lymphocytic cells in varying numbers, and this variation has led to the multiplicity of names. The authors prefer to use the term "thymoma." The non-neoplastic thymus in myasthenia gravis showed varying degrees of involution, and in 75 per cent of the cases the medulla was infiltrated with lymphoid germinal centers. Germinal centers are usually not found in the normal thymus; an occasional germinal center is found in a small percentage of the thymuses of exophthalmic goiter, Addison's disease and acromegaly. Their presence in large numbers almost certainly indicates myasthenia gravis. Although changes in the thymus are the most constant anatomic change in myasthenia gravis, thymectomy has not produced dramatic clinical improvement.

New England Journal of Medicine, Boston

240:445-490 (March 24) 1949

Viral Hepatitis: Consideration of Certain Aspects of Current Importance to Practicing Physician. J. R. Neefe.—p. 445.
Survey of Recent Therapeutic Measures in Cirrhosis of Liver. T. C. Chalmers and C. S. Davidson.—p. 449.
Variations in Hepatic Blood Flow in Man During Health and Disease. S. E. Bradley.—p. 456.
Post-Partum Hematoma. A. W. Lyons.—p. 461.
Tuberculosis. J. D. Wassersug.—p. 463.
Synovioma of Left Knee, with Metastases to Vertebras, Clavicle, Ribs, Pelvic Bones, Peritoneum, Abdominal Lymph Nodes, Lungs and Liver. —p. 472.
Adenocarcinoma of Cecum, with Previous Intussusception.—p. 476.

240:491-528 (March 31) 1949

Survival in Primary Carcinoma of Lung. R. H. Overholt and I. C. Schmidt.—p. 491.
*Pulmonary Embolism: Analysis of 74 Autopsy Cases Since 1941. K. Dehlinger and P. Riemenschneider.—p. 497.
*Serum Potassium Levels in Diabetic Coma. R. H. Sinden, J. L. Tullis and H. F. Root.—p. 502.
Delayed Pneumonia and Urticaria Following Bronchography. H. E. Bass.—p. 505.
Industrial Medicine. I. R. Tabershaw.—p. 508.
Endometriosis of Sigmoid.—p. 517.
Adenocarcinoma, Grade II, of Head of Pancreas, with Metastases to Peritoneum, Liver, Gallbladder, Regional Lymph Nodes, Ileum, Stomach and Lung.—p. 520.

Pulmonary Embolism.—According to Dehlinger and Riemenschneider there has been no significant decrease in the percentage of cases in which pulmonary emboli were demonstrated at necropsy at the New England Deaconess and New England Baptist hospitals since the introduction of definite and prophylactic treatment of venous thrombosis. This therapy includes venous interruption and the administration of heparin and dicumarol,® as well as prophylactic exercises, early ambulation and even paravertebral autonomic block in 1 case. During the thirteen years from 1928 through 1940 pulmonary emboli were found in 7.5 per cent of all autopsies, whereas the figure

became 6.7 per cent during the following six year period. The percentage of operations that were followed by pulmonary embolism, as found at postmortem examination, has decreased somewhat more in the same intervals. Before January 1941 the figure was 0.13 per cent; since that date it has dropped to 0.09 per cent, but even this decrease is not definitely significant statistically. The authors decided to determine why many patients are still dying with pulmonary embolism despite the availability of anticoagulant drugs and the general use of venous interruption in recent years. No analysis of the numerous successfully treated cases was made. Hence, this report should be considered not a condemnation of the methods in use at the present time for the prevention of pulmonary embolism but rather an indication that the problem is still great, even though some of the recent papers lead one to believe that it has been all but completely solved. Seventy-four cases in which necropsy was performed between 1941 and 1946 were analyzed according to age, sex, immediate cause of death, primary site of thrombus, medical versus surgical status and preventive therapy. In only 5 of the 74 cases of pulmonary emboli did the patients receive specific therapy for the prevention of embolism. This suggests that the primary problem is the difficulty in the diagnosis of venous thrombosis and nonfatal pulmonary embolism.

Serum Potassium Levels in Diabetic Coma.—Sinden and associates call attention to the fact that the clinical importance of variations in the serum potassium level during treatment of diabetic coma has been emphasized in many reports. Low potassium values have been observed in certain patients undergoing treatment for diabetic coma, with fatal results unless suitable potassium solutions were administered promptly. Studies of serum potassium levels in shock, cardiac or renal failure indicate that if potassium is given as a therapeutic measure to patients with impending or actual renal failure, a dangerously high level of potassium in the blood serum may also have a fatal result. The physician responsible for the treatment of patients in diabetic coma must have in mind the possibility that critical alterations in the level of blood serum potassium may result in a fatal outcome unless proper treatment is given in an early stage. The causes of a decline in the serum level of potassium from a normal of around 5 milliequivalents per liter to levels of 3 milliequivalents or less are varied. During acidosis, particularly of the diabetic type, there is an immediate and increasing loss of potassium in the urine. This potassium comes chiefly from the cells, through disturbance in cellular permeability which occurs during diabetic coma. The authors present observations on 6 patients with diabetic coma in whom the potassium values were studied routinely. They conclude that in order to prevent dangerously low serum potassium levels in diabetic coma, it is essential that the administration of dextrose be omitted during the first few hours of treatment and that insulin be used in a more aggressive manner.

Northwest Medicine, Seattle

48:171-222 (March) 1949

The Medical Profession as Seen by an Oregon Legislator. R. T. Moore.—p. 174.
Radiation Treatment in Carcinoma of Cervix: Report of Results in 183 Cases. M. Harris.—p. 178.
Accuracy of Pantopaque Studies in Diagnosis of Herniated Intervertebral Disk. S. E. Rees and C. E. Donley.—p. 180.
Hamartoma of Urinary Bladder. T. A. Davis.—p. 182.
Diverticulum of Gastric Cardia. R. S. Smith and J. D. Mortensen.—p. 185.
Surgical Repair of Funnel Chest Deformity. J. K. Poppe.—p. 189.

48:223-292 (April) 1949

Significance and Demonstration of Lobar and Segmental Pulmonary Collapse. J. H. Walker.—p. 241.
Glaucoma and Orally Administered Belladonna. E. V. Ullman and F. D. Mossman.—p. 245.
Ambulatory Electroshock Therapy. H. M. Landberg.—p. 247.
Health Department, Good Servant but Bad Master: Role of Physician in Preserving Individual Freedom. F. B. Exner.—p. 249.
Stevens-Johnson Syndrome with Severe Pulmonary Involvement. R. L. Olsen, C. Barron and J. N. Sledge.—p. 251.
Urethane in Treatment of Chronic Myelogenous Leukemia. R. I. Crone and D. M. Ulrich.—p. 252.
Kielland Forceps: Incidence of Its Use in Review of 1,646 Deliveries. J. C. Brougher.—p. 254.
Endemic Goiter and Cretinism. W. H. Orr.—p. 257.

Oklahoma State Medical Assn. Jour., Oklahoma City

42:87-124 (March) 1949

Ten Years' Progress in Ophthalmology. C. G. Stuard.—p. 90.
Food Infections and Intoxications. F. H. Top.—p. 93.
Problems in Nutrition. Lucile Spire Blachly.—p. 97.
Superficial Foreign Bodies of Cornea. J. H. Goldberger.—p. 100.

42:125-180 (April) 1949

Subtrochanteric Fractures of Femur. C. R. Rountree.—p. 128.
Principles Underlying Management of Renal Calculi. V. Vermooten.—p. 131.
Benign Tumors of Breast. S. N. Stone.—p. 135.
Disease of Scrotal Contents. D. W. Branham.—p. 138.
Cerebral Palsy. O. R. Gregg.—p. 140.

Philippine Medical Association Journal, Manila

25:51-108 (Feb.) 1949

Compensable Illnesses and Injuries: Their Incidence and Prevention. J. S. Santillan and T. V. Ganzales.—p. 51.
Congenital Hydronephrosis. D. Antonio Jr.—p. 61.
Occupational Carbon Monoxide Poisoning: Report of 7 Cases with 2 Fatalities. G. D. Dizon, J. Y. Navarro, V. J. Luciano and others.—p. 67.
Biochemical Studies on Tuberculosis. VI. Diagnostic Significance of Nucleic Acid Test in Tuberculosis. J. F. Leyva.—p. 75.
Early Ambulation. F. V. D'Bayan.—p. 83.

Plastic and Reconstructive Surgery, Baltimore

4:123-224 (March) 1949

Surgical Repair of Decubitus Ulcer in Paraplegics; Further Observations. R. Blocksma, J. G. Kostrubala and P. W. Greeley.—p. 123.
Vascularization of Tubed Pedicles. H. Conway, R. B. Stark and J. P. Docktor.—p. 133.
Method for Repair of Unilateral Cleft Lip. W. H. Steffensen.—p. 144.
Mandibular Reconstruction, World War II. T. G. Blocker Jr. and R. A. Stout.—p. 153.
Cancellous Iliac Bone in Depressions of Forehead, Nose and Chin. D. W. Macomber.—p. 157.
Fundamentals in Surgical Treatment of Mandibular Prognathism. C. W. Waldron, C. I. Karleen and C. A. Waldron.—p. 163.
Metallic Implants and Integrated Artificial Eyes. W. L. Hughes.—p. 175.
Repair of Defects Produced by Excision of Tumors in the Eye Region. K. M. Marcks.—p. 178.
Repair of Full-Thickness Cheek Defects Following Irradiation Necrosis. R. H. Ivy.—p. 188.
Associated Congenital Defects of Ears, Eyelids and Malar Bones (Treacher Collins Syndrome). C. L. Straith and J. R. Lewis.—p. 204.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

70:375-564 (March) 1949. **Partial Index**

Streptomycin in Treatment of Leptospira Carriers. Experiments with Hamsters and Dogs. K. T. Brunner and K. F. Meyer.—p. 450.
Benzene-Inactivated Rabies Vaccine. K. Habel, J. F. Bell and J. T. Wright.—p. 455.
*Rabies Vaccine Freed of Factor Causing Allergic Encephalitis. J. F. Bell, J. T. Wright and K. Habel.—p. 457.
*Aureomycin in Urinary Infections Due to Gram-Negative Organisms. A. M. Rutenburg and F. B. Schweinburg.—p. 464.
Specificity of Differential Sheep Cell Agglutination Test in Rheumatoid Arthritis. S. E. Sulkin, R. M. Pike and H. C. Coggeshall.—p. 475.
Simplified Indirect Complement-Fixation Test Applied to Newcastle Disease Immune Avian Serum. D. M. Wolfe, Lottie Kornfeld and F. S. Markham.—p. 490.
Evaluation of Certain Dangers in Use of Jet Injection Technic. R. V. Brown.—p. 507.
Assay of Secretin and Cholecystokinin Concentrates. L. L. Gershbein, C. C. Wang and A. C. Ivy.—p. 516.
Effect of Zinc on Serum Alkaline Phosphatase Activity in Patients With and Without Cancer. O. Bodansky and Olga Blumenfeld.—p. 546.
*Multiplication of Influenza Virus in Dead Chick Embryos. O. Lahelle and F. L. Horsfall Jr.—p. 547.

Rabies Vaccine Freed of Factor Causing Allergic Encephalitis.—Bell and associates present a method for the removal from rabies vaccine of the factor which causes allergic encephalomyelitis. This factor is not removed by extraction with benzene and ether, but preliminary treatment of the vaccine with these solvents facilitates separation by subsequent treatment. The presence of calcium acetate prevents the loss of antigen when the vaccine is washed. It does not prevent removal of the encephalitic factor which appears to be water soluble. About one half of the total nitrogen of the vaccine is removed by this washing process. The technic is as follows: 1. A suspension of infected brain in water is dried from the frozen state. 2. The dried brain is extracted with benzene followed by ether (live virus may be killed in this stage by heating in benzene). 3. After removal of the ether the dried

brain is suspended in distilled water. 4. Sufficient solution of calcium acetate is added to make final concentration of tenth-molar calcium acetate, and the suspension is permitted to stand in the cold for an hour or two. 5. The calcium acetate solution is removed by centrifugation or infiltration, and the sediment is resuspended in distilled water to the original volume with agitation (clumps of sediment must be broken up). 6. The distilled water is removed by centrifugation or filtration. 7. The sediment is resuspended in distilled water or saline solution and homogenized.

Aureomycin in Urinary Infections.—According to Rutenburg and Schweinburg aureomycin is highly effective against many strains of gram-negative bacilli in vitro, including many which were found to be resistant to sulfonamide drugs, penicillin and streptomycin. The sensitivity of various strains of a given species varies greatly. Clinical trial in 10 patients with urinary infections which were refractory to previous treatment with other antibiotics resulted in a clinical cure of all 10 patients. Bacteriologically, 8 patients were cured and 2 were greatly improved.

Multiplication of Influenza Virus in Dead Chick Embryos.—Lahelle and Horsfall performed experiments in which time and temperature at which embryos were held were varied over wide ranges. The result obtained indicate that the PR8 strain of influenza A virus is capable of multiplication in the tissues of dead chick embryos if incubation at 35 C. is sufficiently prolonged. The virus multiplies in dead embryos to an extent comparable to its multiplication in the living embryo. These results may be of practical usefulness, especially in field work. When adequate laboratory facilities are lacking, dead embryos which have been stored for considerable periods may prove satisfactory for the recovery of the infectious agent.

Psychiatry, Washington, D. C.

12:1-104 (Feb.) 1949. **Partial Index**

Theory of Anxiety and Nature of Psychotherapy. H. S. Sullivan.—p. 3.
Management of Type of Institutional Participation in Mental Illness. A. H. Stanton and M. S. Schwartz.—p. 13.
Anxiety and Guilt in the Modern Community. W. Line.—p. 27.
Dynamics in Hypnotic Induction. J. A. Christenson Jr.—p. 37.
Study of Mothers of Schizophrenic Patients. T. Tietze.—p. 55.

Psychosomatic Medicine, New York

11:1-68 (Jan.-Feb.) 1949

Emotional Factors in Etiology of Hyperthyroidism: Report of Preliminary Survey.—p. 2.
Physiologic Studies of Reaction to Stress in Anxiety and Early Schizophrenia. R. B. Malmo and C. Shagass.—p. 9.
Physiologic Study of Symptom Mechanisms in Psychiatric Patients Under Stress. R. B. Malmo and C. Shagass.—p. 25.
Effect of Chronic Fear on Gastric Secretion of HCl in Dogs. G. F. Mahl.—p. 30.

South Dakota Journal of Medicine, Sioux Falls

2:75-114 (March) 1949

The Bacteriologist Considers Drug-Fastness. R. P. Elrod.—p. 75.
Cancer of Breast. W. C. White.—p. 79.
*Idiopathic Ulcerative Colitis. C. Dennis.—p. 83.

2:115-152 (April) 1949

Benign Tumors of Breast and Associated Conditions. M. M. Copeland.—p. 116.
Exfoliative Cytology. R. L. Ferguson.—p. 124.
Pathologic Diagnosis of Cancer. E. DeCoursey.—p. 126.

Idiopathic Ulcerative Colitis.—Dennis states that many patients may be satisfactorily treated with nonsurgical regimens alone. In the experience at the University of Minnesota, where the cases are more highly selected, more than three fourths are treated surgically. At present, patients with fulminating disease and those of relatively early disease are treated by vagotomy when medical measures have not produced subsidence of the disease within four weeks. Patients who have had the disease longer than three weeks and patients who do not respond well to vagotomy should have ileostomy and colectomy. If the rectum is not removed, it must be examined every four months because of the risk of cancer formation.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

22:183-242 (April) 1949

Symposium on Small Field X-Ray Therapy for Deep-Seated Tumors, with Special Reference to Rotation Technics. P. R. Steed and others.—p. 185.
Use of X-Ray Films in Beam Direction for X-Ray Therapy. W. A. Copcutt.—p. 210.
Note on Klein-Nishina Formulas for Compton Scattering of Photons by Electrons, with Table. R. K. Appleyard and D. J. Allen-Williams.—p. 215.
*Use of CO_2 and Air as Antispasmodics. P. Cave.—p. 216.
Bronchography—Methods by Which It May Be Performed and Factors Influencing Choice of Method Employed: Part II. A. A. Vickers.—p. 224.
Home-Made Viewing Box Employing Fluorescent Illumination. J. Aspin.—p. 234.

Use of Carbon Dioxide or Air as Antispasmodics.—Cave points out that in gastrointestinal radiography spasm is common either alone or combined with organic disease, and its elimination as a cause of narrowing is an important step in diagnosis. Not infrequently the radiologist may have serious doubts as to whether narrowing is of spastic or organic origin. A simple, efficient and rapid method of relieving spasm in the alimentary tract is of considerable practical importance. Inflation of parts of the alimentary tract by air or carbon dioxide generated by effervescent substance may be of value in differentiating between alterations of the lumen due to spasm and those due to organic change. The increase of pressure readily abolishes spasm, but infiltrations of the wall remain undistended. Inflation of the esophagus or stomach is easily achieved with the use of compound effervescent powders (Seidlitz powders). The method has proved useful in overcoming pylorospasm. The employment of air contrast in the colon is well established, but its value as an antispasmodic is less appreciated.

British Medical Journal, London

1:603-644 (April 9) 1949

Medical Fitness for Air Travel. H. Whittingham, A. B. Barbour and J. C. Macgown.—p. 603.
Physiological Basis of Vagotomy. A. D. Beattie.—p. 607.
Notes on Experiments Illustrating Normal Temperature Regulation in Young Men. S. Wright.—p. 610.
Use of Diparcol in Parkinsonism. R. S. Duff.—p. 613.
Successful Treatment of Typhoid Carrier with Penicillin and Sulphamerazine. C. A. Rumball and L. G. Moore.—p. 615.
"Myanesin" in Treatment of Tetanus. M. H. A. Davison, A. B. Ward and E. A. Pask.—p. 616.
"Minor" Injury of Terminal Phalanx. F. I. Powell.—p. 618.

East African Medical Journal, Nairobi

26:31-56 (Feb.) 1949

Leprosy in Kenya. J. R. Innes.—p. 32.
*Cutaneous Cancer in Kenya. F. Piers.—p. 36.

Cutaneous Cancer in White Population in Kenya.—Piers says that of the 51 patients with cutaneous cancer seen by him since 1941, 27 gave a history of long occupational exposure to sun and 10 others, whose occupation did not suggest such exposure, gave a past history of such exposure. Only 14 patients gave no history of exposure to sun light. Chronic sunburn was present in 34 patients, permanent suntan in 3, farmer's skin in 18 and chronic solar dermatitis in 13. Among the European residents of Kenya cutaneous cancer is second in frequency only to breast cancer. The habit of dispensing with the sun helmet altogether and of participating in outdoor activities and sports without adequate protection is widespread among the younger generation in Kenya. The danger inherent in this careless exposure is not realized by the public. There is little hope that reasonable arguments will prevail against the fashionable craze of modern sun worship. The amount of sun light required for the production of vitamin D is small; it can be obtained by limited exposure even in temperate climates. In the tropics the effects of prolonged insolation are eventually injurious rather than beneficial. The risk of cutaneous cancer can be easily decreased by the regular application of protective creams and by the wearing of hats and suitable light clothing.

Journal of Laryngology and Otology, London

68:107-178 (March) 1949

The End of an Era: Retrospect and Prospect. W. Howarth.—p. 107.
*Septicemia After Tonsil Operations. E. W. Williams.—p. 115.
Evolution of Auditory Conducting Apparatus: I. New Theory Based on Functional Considerations. A. Tumarkin.—p. 119.
Observations on Antro-Choanal Polypus. A. R. Dingley.—p. 141.
Clinical Aspect of Perceptive Deafness—So-Called Nerve or Internal Ear Deafness. E. D. D. Davis.—p. 144.

Septicemia After Operations on Tonsils.—According to Williams acute septicemia after tonsil operations is rare. Among 10,000 tonsillectomies performed by him, there were only 2 cases of septicemia. At least twice that number had been performed by others at his hospital during the same period with 2 instances of septicemia. Of the 4 cases reported, 2 had a fatal outcome. The most striking features of the condition are vomiting, diarrhea and collapse. It is interesting that this rare complication has been recorded three or four times in pairs, each pair composed of 2 small children from the same family. If the explanation is that in each pair acute streptococcic tonsillitis was imminent, it is difficult to see how these accidents can be avoided and why there have not been more numerous isolated examples of this complication.

Lancet, London

1:593-636 (April 9) 1949

Treatment of Congestive Heart-Failure. H. A. Reid and W. Hughes.—p. 593.
*Subcutaneous Implantation of Insulin in Diabetes Mellitus. L. Vargas.——p. 598.
Complete Rupture of Membranous Urethra. A. H. Hunt and C. N. Morgan.—p. 601.
Filamentous Forms Associated with Newly Isolated Influenza Virus. C. M. Chu, I. M. Dawson and W. J. Elford.—p. 602.
Role of Di-Isopropyl Fluorophosphonate in Surgery. J. P. Quilliam and T. A. Quilliam.—p. 603.
Operation for Severe Varicose Veins During Pregnancy. H. Dodd.—p. 606.
Mortality from Pink Disease in 1923-47. W. P. D. Logan.—p. 608.

Implantation of Insulin in Diabetes Mellitus.—Vargas cites earlier investigations by himself and associates which proved that pellets of protamine zinc insulin complex mixed with cholesterol gave up their insulin slowly when they were implanted in normal rabbits. He reports results obtained in the first 7 patients treated by this new method. It was proved in these 7 patients that pellets of protamine-zinc-insulin-cholesterol implanted subcutaneously are absorbed as slowly as fat-soluble hormones. The dose used in the implant varied from 20 to 92.7 units of insulin per kilogram of body weight, except in 1 case in which 450 units was given. It was calculated, in accordance with experimental data, that the daily absorption of the implant was about 1 per cent, which seems to be confirmed by the present cases. This assures a maximum duration of activity of the implant of about one hundred days. The author considers the method of implanting pellets of insulin extremely promising and worth further study in a larger number of patients.

Medical Journal of Australia, Sydney

1:225-246 (Feb. 19) 1949

Intestinal Obstruction in Infants: Challenge. A. M. Clarke.—p. 225.
Hand Injuries. B. K. Rank.—p. 228.
Head Injuries in Civil Practice. L. Lindon.—p. 231.
Value of Albumin-Fortified Anti-Rh Serum for Rh Testing. V. I. Krieger.—p. 233.

1:289-332 (March 5) 1949. **Partial Index**

Nervous and Chemical Control of Uterus. F. A. Maguire.—p. 289.
Brief Summary of Indications for Methods of Induction of Labor. T. D. Hughes.——p. 291.
Complications and Results of Induction of Labor. T. H. Small.—p. 292.
Vaginal Hysterectomy-Colporrhaphy. A. L. Watson.—p. 297.
Treatment of Ankylosing Spondylitis and Osteoarthritis. F. Duval.—p. 301.
Osteoarthritis of Hip: Surgical Treatment. J. Hoets.—p. 303.
BCG Vaccine. E. A. North.—p. 306.
Epidemiology of Primary Herpes Simplex Infection. S. G. Anderson and J. Hamilton.—p. 308.
Ocular Prosthesis, with Special Reference to Conjunctival Sac. D. B. Waugh.—p. 311.
Some Clinical Aspects of Water Balance. J. G. Hislop.—p. 313.

South African Medical Journal, Cape Town

23:221-240 (March 26) 1949. **Partial Index**

Thyrotrophic Exophthalmos. C. J. B. Muller.—p. 221.
*Acute Toluene Poisoning. J. B. Lurie.—p. 233.

Acute Toluene Poisoning.—Lurie reports the case of a man who had to clean the inside of a tank, the sides and floor of which were coated with an emulsion of DDT containing 45 per cent pure toluene. The floor of the tank contained about six inches of water placed there for cleaning purposes. The man, wearing a respirator, was lowered into the tank and immediately removed the respirator. He then commenced sluicing the sides of the tank. Two other men wearing respirators, while awaiting their turn to be lowered into another tank, were watching. They noticed the man in the tank collapse after he had been working for approximately fifteen minutes. They pushed the man into the fresh air, where he recovered consciousness after artificial respiration had been given for a few minutes. He was taken to a hospital. His overalls, which were sodden with DDT emulsion, were removed. He stagged around and appeared to be extremely irritable, restless, disoriented and excited. About three hours after the incident, he appeared semicomatose, rather restless, only slightly disoriented and quiet rather than excited. He was not able to answer questions rationally. He was dyspneic, and examination of the chest revealed generalized rales and rhonchi, with evidence of excessive mucus in the bronchi. The treatment included measures to counteract shock and penicillin sodium therapy. A week later the lungs were clear. The condition in this case was diagnosed as acute toluene poisoning; nevertheless, poisoning with DDT, though remote, had to be excluded. No case of DDT poisoning has so far been described where symptoms and signs manifested themselves fifteen minutes after exposure. The toxicity of toluene in its acute form is chiefly related to the central nervous system. The affinity of benzene and toluene for the lipase substances present in the cells of the central nervous system will produce symptoms characteristic of inebriation, narcosis and endogenous psychosis. Headache, vertigo, nausea, fatigue and giddiness will be the predominant complaints and disturbance of equilibrium (with a positive Romberg's sign), ataxia, paresthesia and staggering gait the chief signs. Psychotic disturbances will manifest themselves in restlessness, disorientation, loss of memory, fugues, hallucinations and irritability, culminating in loss of consciousness. The wearing of respirators should be rigidly enforced in those working for even a short period in heavy concentrations of benzene and toluene.

Transactions Royal Soc. Trop. Med. and Hyg., London

42:417-510 (March) 1949. **Partial Index**

Some Observations on Action of Quinine, Atebrin, and Plasmoquine on Plasmodium Vivax. M. J. Mackerras and Q. N. Ercole.—p. 443.
Observations on Action of Quinine, Atebrin and Plasmoquine on Gametocytes of Plasmodium Falciparum. M. J. Mackerras and Q. N. Ercole.—p. 455.
Studies on West African Strain of Plasmodium Falciparum: II. Efficacy of Paludrine (Proguanil) as Therapeutic Agent. G. Covell, W. D. Nicol, P. G. Shute and M. Maryon.—p. 465.
Chronic Pulmonary Schistosomiasis: Clinical and Radiologic Study. M. Erfan, H. Erfan, A. M. Mousa and A. A. Deeb.—p. 477.
*Treatment of Polycythemia Vera: Record of 1 Case Treated with Ancylostoma Infection. H. F. Nagaty and A. F. Zanaty.—p. 493.

Treatment of Polycythemia Vera by Artificial Infection with Ancylostoma Duodenale.—Nagaty and Zanaty present the case of a man, aged 55, who had polycythemia vera. They attempted to produce in him helminthic anemia by inducing infection with Ancylostoma duodenale. This treatment was tried for the first time by Duvoir in 1940. The authors' case is the second in which treatment by Ancylostoma infection is described. They describe how the Ancylostoma larvae were obtained, how they were applied and the results of the blood tests made from time to time after the introduction of infective Ancylostoma larvae. On the date of the last examination, about eighteen months after Ancylostoma larvae had first been introduced, the red cell count was normal and the hemoglobin level had fallen to 60 per cent; the total leukocyte count was still high, with pronounced eosinophilia. The patient felt and looked better. There was no giddiness, headache or palpitation on exertion; his pulse rate was 75 per minute, and he could walk

better and for longer periods. His color was normal, and there was no congestion of the skin or engorgement of the face. He was more energetic and did his regular job efficiently. The authors list the advantages of treating polycythemia by artificial infection with Ancylostoma duodenale.

Acta Tuberculosea Scandinavica, Copenhagen

23:1-122 (No. 1) 1949

*Diagnostic BCG Test. H. J. Ustvedt and A. Aanonsen.—p. 1.
Further Investigations on Pathogenesis of Renal Tuberculosis: Relation Between Pulmonary and Urogenital Tuberculosis. H. J. Ustvedt and H. Wergeland.—p. 36.
Pathogenesis of Pulmonary Tuberculosis. R. H. Dahl.—p. 63.
Studies on Inflammation: Investigations into Bacterial Fixation at Site of Inflammation. U. Voigt.—p. 79.

Diagnostic BCG Test.—Ustvedt and Aanonsen show that tuberculin tests may fail in the presence of tuberculosis and occasionally elicit positive results (nonspecific reactions) in the absence of the disease. They feel that increasing the dose of tuberculin in the Mantoux test beyond 1 mg. will lead to the production of too many nonspecific reactions. Other methods must be found for separating the infected from the noninfected within the tuberculin-negative group and for distinguishing between specific and nonspecific reactions. They suggest that in tuberculin-negative persons and those with a negative Pirquet reaction and a positive Mantoux "early reaction" to cutaneous application of BCG may be employed in order to single out among tuberculin-negative persons those who, in spite of tuberculin negativity, harbor a tuberculous infection and to distinguish between specific and nonspecific Mantoux reactions in the Pirquet-negative but Mantoux-positive patients. The test is carried out by means of two punctures in the skin through a drop of BCG containing 20 mg. per cubic centimeter; the results ought to be read after six days. Distinct formation of papules indicates specific reaction, which is designated positive early reaction to BCG. The test ought further to be employed in persons vaccinated with BCG who show tuberculin negativity after vaccination, and by means of follow-up investigations it should be ascertained whether positive early reaction to BCG constitutes a sufficient criterion of immunity.

Archivio Italiano di Chirurgia, Bologna

71:71-146 (No. 2) 1949. **Partial Index**

*Experiments on Blood Transfusion: Elimination of Bile Pigments After Transfusion of Preserved Blood and of Plasma. V. Laudicella.—p. 85.

Transfusion of Blood or Plasma.—Laudicella bled dogs, removing the amount of blood which corresponded to the amount of blood or plasma to be transfused. Bilirubin elimination was measured with the aid of an internal biliary fistula. Transfusion of large quantities of blood, either fresh or conserved, increases the elimination of bilirubin in proportion to the amount of bilirubin yielded by destruction of all transfused erythrocytes. Post-transfusion hemolysis is of longer duration after transfusion of preserved blood than after transfusion of fresh blood. Transfusion of small quantities of fresh blood elicits only mild hemolysis, which shows that part of the transfused erythrocytes are used by the blood. Plasma infusion does not cause hemolysis. The author suggests plasma infusions combined with repeated transfusions of small quantities of fresh blood instead of large blood transfusions.

Medizinische Klinik, Munich

44:225-256 (Feb. 25) 1949. **Partial Index**

*Results Obtained with Thiosemicarbazone Therapy of Tuberculosis. H. Malluche.—p. 225.
Case of Periarteritis Nodosa; Demonstration of Vasoconstrictor Effect of Patient's Serum. W. D. Germer.—p. 231.
Morphologic Investigation on Shock, Collapse and Fat Embolism. W. Gloggengiesser.—p. 235.
Question of Conservative Treatment of Senile Cataract. W. Straub.—p. 239.

Thiosemicarbazone in Tuberculosis.—Malluche treated 50 patients with exudative pulmonary tuberculosis with thiosemicarbazone. One tablet, containing 0.125 Gm. of thiosemicarbazone and 0.125 Gm. of sulfathiazole, was given daily by mouth. Treatment was continued for several months. In 7 patients with severe pulmonary tuberculosis, combined with tuberculosis of the colon in 6 and with tuberculous empyema of the knee joint in 1, considerable clinical roentgenologic improvement was obtained and the prognosis was definitely improved. Fifteen patients showed only temporary clinical and roentgenologic improvement without change in the prognosis; in 14 patients (28 per cent) with severe pulmonary tuberculosis, 1 of them with suppurating tuberculosis of the thoracic vertebrae and transverse paralysis, there was little and only temporary improvement without change in prognosis, and 3 patients died; in 4 patients there was only a delay in the fatal course of their disease; treatment failed in 7 patients, and 3 patients had not been treated long enough for correct evaluation. In 20 patients the temperature was restored to normal and the amount of sputum was reduced. In patients in whom other organs in addition to the lungs were involved, the extrapulmonary tuberculosis showed better and more rapid improvement than the pulmonary tuberculosis. Results were best in intestinal tuberculosis, the patients gaining considerably in weight. Resolution of infiltration was the primary effect of the treatment in pulmonary tuberculosis. Untoward reactions consisted of headache, anorexia, nausea, vomiting, epistaxis and choked disk, but only occasionally were these severe enough to require that treatment be discontinued. Thiosemicarbazone is a chemotherapeutic agent with a specific effect on Koch's bacillus; in intestinal tuberculosis the effect is superior to that of any other drug.

44:485-512 (April 22) 1949. **Partial Index**

*Roentgen Rays in Treatment of Oliguria and Anuria. R. Heintz.—p. 496.
Diagnosis of Parathyroid Insufficiency. E. L. Schäfer.—p. 500.
*Peptic Ulcer and Sympathetic Nervous System. K. Nitsch.—p. 503.
Late Edema in Presence of Normal Albumin Content. H. Gros.—p. 511.
Short Alkaline Tolerance Test as Method for Detection of Acidosis. H. Böttner and H. Linden.—p. 514.
Clinical Report on Testosterone Therapy of Carcinoma of Breast. W. Jorde.—p. 516.

Roentgen Therapy in Anuria.—The first of the 3 patients presented by Heintz was a woman, aged 51, who had been treated with sulfonamide drugs in the course of a virus pneumonia that had begun with an influenza-like process. Oliguria and anuria with renal insufficiency and acute uremia developed. Application of heat to the kidneys, infusion of sodium chloride, the forcing of water and paravertebral anesthesia were ineffective. Application of roentgen rays to the region of both kidneys was followed by a period of polyuria with improvement in the concentration capacity of the kidney and subsidence of the secretory blockage. In the 2 other cases anuria developed in the course of glomerulonephritis. Here again roentgen therapy counteracted the anuria. The author suggests that the anuria resulted from spasms in the interlobular arteries and that the roentgen treatment had a spasmolytic effect on them. The roentgen rays probably exerted their influence by way of the sympathetic nervous system.

Peptic Ulcers and Sympathetic Nervous System.—The observations reported by Nitsch were made in a military unit in which men subject to recurrent gastric disorders had been grouped together. Among the 850 men with chronic gastric disorders there were 324 who had had at least 2 ulcer attacks within the preceding thirty months. These men belonged to a coast guard unit and received the same type of diet, which was not greatly restricted. Alcoholic drinks and smoking had been forbidden. Physical exertion and hours of sleep were similar for all. These 324 men were divided into three groups on the basis of the alphabetic order of their names (in rotation, 1 to each group). Average ages and weights were similar in the three groups. The men in group 1 received no medication; those in group 2 were given 1 tablet of bellergal (a preparation containing ergotamine tartrate, bellafolin® [a preparation of belladonna alkaloids] and phenobarbital) three times daily and also 1 tablet of phenobarbital three times daily. Those of group 3 were given this medication only when they were losing weight (more than two thirds of a pound [0.33 Kg.] a week) or when there was a noticeable increase in sympathetic dystonia. Subjectivism was avoided, in that the physician did not know what group a man belonged to; the men did not know why they had to take the tablets. Recurrences of ulcer appeared in 38 men of group 1, in 6 of group 2 and in 13 of group 3. Weekly control examinations revealed that the subjective symptoms that accompany a recurrence of ulcer usually

are preceded for a week or two by signs of increased sympathetic dystonia. In evaluating whether the medicinal treatment which under these conditions was begun in group 3 was effective in preventing a relapse, the author says that during a four month period the relapse rate was 17 in group 1 and 10 in group 3. The purpose of the study was to determine whether the tendency to relapse could be reduced by influencing the sympathetic nervous system by drugs that act on the brain stem. The observations indicate that the sympathetic nervous system plays an important role in ulcer recurrence.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

93:541-616 (Feb. 19) 1949. **Partial Index**

*Mechanical Heart-Lung System. J. Jongbloed.—p. 548.
Investigation of Causes of Death in 200 Stillborn Infants. B. S. ten Berge and G. Linthorst.—p. 553.

Mechanical Heart-Lung System.—On the basis of experiments in dogs with a mechanical device which takes over the function of the heart and lungs, Jongbloed constructed a heart-lung system with a capacity suitable for human subjects. He describes this apparatus, the most important part of which is a new type of artificial lung, the spiral oxygenator. In experiments on large dogs (over 30 Kg.), in which only half of the apparatus was in use, this new mechanical heart-lung system came up to all expectations.

93:617-692 (Feb. 26) 1949. **Partial Index**

*Development of Gallstones After Gastric Resection for Ulcer. C. L. H. Majoor, T. J. J. Suren and M. M. Madlener.—p. 626.
Insufficiency of Sphincter of Oddi. H. van Ijzeren.—p. 631.

Gallstones After Gastric Resection.—Majoor and associates present the case of a woman, aged 47, who underwent gastric resection for duodenal ulcer. About two months after the operation she complained of colicky pains in the upper part of the abdomen. Roentgenologic examination of the gallbladder showed small, "swimming" stones, which had not been present before the operation on the stomach. This supports the view that the Billroth II resection may promote the formation of gallstones. Numerous small stones were found in the gallbladder as well as white, sugar-like crystals of cholesterol. These crystals represent probably the first phase in the morphogenesis of gallstones.

93:769-844 (March 12) 1949. **Partial Index**

Sympathetic Reactions Caused by Stimulation of Labyrinth. J. Hulk and H. E. Henkes.—p. 783.
*Denervation of Joints in Arthritis Deformans. E. A. Immink.—p. 791.
Case of Amebic Hepatitis. J. M. Cannoo.—p. 799.

Denervation of Joints in Arthritis Deformans.—Immink shows that degenerative, toxic-infectious and constitutional factors are involved in arthritis deformans. It was Tavernier who suggested that pain caused by this process be counteracted by denervation of the involved joint. In some instances the author combined Tavernier's denervation with Chapchal's paravertebral sympathetic block. His results in the denervation of twenty hip joints were good (disappearance of pain and great improvement in mobility) in 13 cases, fair (disappearance of pain and some improvement in movement) in 5 and in the other 2 there was no improvement. The denervation of nineteen knee joints gave good results in 11 cases, fair results in 6 and effected no improvement in 2 cases.

Presse Médicale, Paris

57:353-364 (April 20) 1949. **Partial Index**

*Treatment of Tuberculosis in Early Infancy with Streptomycin. J. Cathala, P. Auzépy, R. Bastin and J. Hartmann.—p 353.
Retarded Penicillin. New Preparations Used for Treatment of Gonorrhea. C. Levaditi, H. Penau, A. Vaisman and G. Hagemann.—p. 355.
New Retarded-Penicillin Preparations for Treatment of Experimental and Human Syphilis. C. Levaditi, H. Penau, A. Vaisman and G. Hagemann.—p. 356.
Contribution to the Study of Topectomy. M. Feld and R. Messimy.—p. 358.

Streptomycin in Tuberculosis of Infants.—Cathala and co-workers report on two years' experience with streptomycin in the treatment of tuberculosis in early infancy. Eighteen infants between 6 months and 3 years of age with tuberculous meningitis were given daily intraspinal injections of 2.5 cg. of the drug for ten to twelve days; later these injections were given twice or once per week. In addition, the infants were given daily 5 cg. of the drug per kilogram of body weight in two injections at twelve hour intervals. Twelve infants died. Three patients were alive and normal, seventeen months, seven months and one month, respectively, after treatment was discontinued; 2 patients were in good condition, but treatment had not been discontinued at the time of reporting. Fifty-two infants, between 2½ months and 3 years of age, 11 with caseous types of pulmonary tuberculosis, 7 with miliary tuberculosis, 14 with primary complex and involvement of juxtatracheal lymph nodes, 16 with primary complex and a favorable prognosis, 3 with tuberculosis of the bones and 1 with tuberculous mastoiditis were given daily doses of 3 to 5 cg. of the drug per kilogram of body weight for six to twelve weeks. Twelve patients died and 40 recovered. Among those that recovered were 3 with miliary tuberculosis and 4 with bronchopulmonary tuberculosis in whom multiple nodules were demonstrated on roentgenologic examination. Treatment with streptomycin proved successful in patients regarded as incurable. Results varied, and treatment was prolonged, painful and expensive. Although complete sterilization of the organism does not seem likely to be achieved, treatment with the drug is advisable for all types of tuberculosis in early infancy, because a primary infection with a grave prognosis may be converted into a benign primary infection permitting the patient to acquire permanent immunity.

Revista Argentina de Reumatología, Buenos Aires

13:262-284 (March) 1949. **Partial Index**

*Treatment of Rheumatoid Arthritis. M. Losada L. and O. France S.—p. 274.

Treatment of Rheumatoid Arthritis.—Losada and France employed a gold preparation in 136 adult patients with rheumatoid arthritis. Results are recorded in 60 patients given intramuscular injections of sodium gold thiosulfate in doses of 0.01 Gm. with intervals of six days for a first course of five injections followed by injections of 0.05 Gm. of the drug with intervals of fifteen, twenty or thirty days. The disease had existed less than one year in 13 patients and between two and ten years in the remaining patients. Cure was obtained in 19 patients and improvement in 17. In the remaining patients either the treatment had failed or the results were unknown to the authors. Toxic, acute reactions occurred in 20 patients, in 9 of whom the treatment had to be discontinued. Sodium gold thiosulfate therapy is of value in rheumatoid arthritis provided it is administered early in the course of the disease and for a period varying between one or two years. Hepatic, intestinal, renal, blood and skin disease, cardiac insufficiency, asthma, grave diabetes and pregnancy are contraindications. Gold therapy gives mediocre results in patients with spondyloarthritis and with Still-Chauffard and Felty's syndrome.

Semaine des Hôpitaux de Paris

25:755-796 (March 6) 1949. **Partial Index**

Chair of Rheumatology; Inaugural Lecture. F. Coste.—p. 755.
Plasmocyte Leukosis; Comparison with Kahler's Disease and Leukoblast Leukosis. P. Milliez and J. Mallarmé.—p. 763.
*Aspiration Liver Biopsy by Transthoracic Route. L. Bertrand.—p. 769.
*Subcutaneous and Cutaneous Vaccination with BCG, 1926 to 1948. J. Heimbeck.—p. 771.

Aspiration Liver Biopsy.—Bertrand performed 34 aspiration liver biopsies in eight months on patients with miliary pulmonary tuberculosis who had been treated with streptomycin. On admission some of these patients presented moderate hypertrophy of the liver. More often the liver was normal in size or rapidly became normal with streptomycin therapy. The site of insertion of the needle was either the seventh or the eighth intercostal space in the anterior axillary line. Liver puncture was done with local anesthesia with 10 cc. of a 1 per cent solution of procaine hydrochloride. The cannula used was 16 cm. in length, 1.5 to 2 mm. in width and fitted with a trocar. The bleeding, clotting and prothrombin times were determined before the puncture. Scapular radiating pain may be experienced in the course of puncture and may persist for several hours, but it seldom requires opiates. The exploration is usually painless.

Puncture never failed in the author's cases. Hemorrhage of the liver did not occur. It can be prevented by a correct technic and by a routine follow-up of the hemostatic status of the patient. In 2 patients the liver was approached through a therapeutic pneumothorax without any difficulty.

BCG Vaccination.—Heimbeck reports on BCG vaccination in two groups during the period 1926-1948. One group consisted of student nurses aged about 20, whose activities and living conditions were similar and who were heavily exposed to tuberculosis. The other was a population group of Oslo, Norway, whose members differed considerably with regard to age and living conditions and were exposed to the common tuberculous infection, which as a rule does not affect more than 2 to 3 per cent of the population per year. In the early years of the employment of this method of vaccination a single dose of 0.05 to 0.10 mg. of the vaccine was injected subcutaneously. Because of the frequent occurrence of an abscess at the site of the injection the subcutaneous route was replaced by the cutaneous route. The vaccine dose of 0.1 mg. was divided in three to five small superficial injections, which produced small anemic papules on the epidermis. Of 501 vaccinated nurses, with a total number of 4,958 years of observation, 49 (9.9 per cent) acquired tuberculosis and 5 (1 per cent) died per 1,000 years of observation. Of 668 nonvaccinated nurses, with a total number of 7,449 years of observation and with a positive Pirquet reaction, 39 (5.2 per cent) acquired tuberculosis and 1 died (0.1 per cent) per 1,000 years of observation, while of 284 nonvaccinated nurses, with 2,563 years of observation and a negative Pirquet reaction, 106 (41.4 per cent) acquired tuberculosis and 12 died (4.2 per cent) per 1,000 years of observation. Thus the immunity obtained by BCG vaccination reduced the morbidity and mortality rate by one fourth, but the immunity produced by the vaccine was less effective than that resulting from a primary infection. Of 842 persons of the population of Oslo who were vaccinated, 9 (1.6 per cent) acquired tuberculosis and none died per 1,000 years of observation. Of 2,836 persons with a negative Pirquet reaction, 190 (8.8 per cent) acquired tuberculosis and 13 (0.6 per cent) died per 1,000 years of observation, while of 2,421 persons with a positive Pirquet reaction 54 (2.7 per cent) acquired tuberculosis and 6 (0.3 per cent) died per 1,000 years of observation. BCG vaccination reduced the morbidity and mortality rate under common conditions of infection to one fifth of that of the nonvaccinated persons. Today BCG vaccine is the best agent for combating tuberculosis.

Ugeskrift for Leager, Copenhagen

111:55-82 (Jan. 20) 1949

Gamma Globulin and Its Clinical Application. Review. A. Hansen and B. Jordal.—p. 55.
*Gamma Globulin in Prophylaxis Against Measles. B. Jordal.—p. 59.
Apparatus for Ambulant Traction Treatment. H. Sørensen.—p. 63.

Gamma Globulin in Prophylaxis Against Measles.—Because of the inadequate supply of measles convalescent serum in Denmark late in 1947, human gamma globulin was prepared and issued interchangeably with convalescent serum in the 1947-1948 measles epidemic. Jordal says that injection of gamma globulin within six days after the first contact gave 91.3 to 93.7 per cent protection and administration of convalescent serum within the same time after contact gave 96.4 to 100 per cent protection. The dosage of gamma globulin was that used in the United States.

111:113-138 (Feb. 3) 1949. **Partial Index**

*Change in Operative Mortality After Suture of Perforated Gastric Ulcer. J. C. Christoffersen and J. Mortens.—p. 113.
Cervical Sympathetic Block in Humeroscapular Periarthrosis with Secondary Reflex Dystrophy. K. Jespersen.—p. 119.

Change in Operative Mortality After Suture of Perforated Gastric Ulcer.—Christoffersen and Mortens' material comprises 213 cases in which there was surgical treatment for repair of perforated gastric ulcer from 1929 to 1948. The operative mortality was reduced from 40 deaths (28 per cent) in the 145 patients treated from 1929 to 1944 to 3 (4 per cent) in the 68 treated from 1945 to 1948. The operative technic was unchanged. Examination of the causes of death from 1929 to 1944 and from 1945 to 1948 shows the great value of sulfonamide drugs and penicillin and of the modern methods of anesthesia and intensive preoperative and/or postoperative treatment of shock which allow the full effect of these agents to be utilized. The importance of immediate availability of sufficient blood (or blood substitutes) for transfusion is stressed.

111:165-200 (Feb. 17) 1949

*Prolapse of Lumbar Disk. E. Busch, A. Andersen, B. Broager and others.—p. 165.
Suggestion for New Technic in Urinalysis. P. E. Oswald.—p. 188.

Prolapse of Lumbar Disk.—Busch and his associates say that prolapse of the lumbar disk is common and is the most frequent cause of lumbago-sciatica with symptoms of radicular compression. Of 1,000 verified cases of lumbar disk prolapse 50.8 per cent were those of the fourth lumbar disk and 41.3 per cent of the fifth lumbar disk. Prolapses may be multiple. Heavy physical work and trauma play a part in the development of the prolapse. In fully half the cases a probable causative trauma was established. The prolapse and its localization can usually be diagnosed on roentgen and clinical examination; myelography is necessary in about 10 per cent of the cases. In most cases operation is not needed. The indication for operative treatment depends on the part the prolapse and its symptoms play in the patient's life. Operation is often indicated in cases with objective signs of radicular compression with sensory or motor loss which do not disappear quickly. The operative indication becomes absolute in cases with extensive compression and spinal block. Follow-up of 738 patients after partial hemilaminectomy, hemilaminectomy, laminectomy or transligamentary operation showed good results in 70 per cent, improvement in 18 per cent, unsatisfactory results in 10 per cent. The unsatisfactory results were mainly due to cicatricial root compression, radiculitis, instability of the affected lumbar disk, miosis and neurosis.

Wiener medizinische Wochenschrift, Vienna

99:161-186 (April 9) 1949

Adams-Stokes Syndrome. O. Zimmermann-Meinzingen.—p. 161.
Histopathology of Ganglion Cells of Sympathetic Trunk in Man. F. Feyrter.—p. 164.
Treatment of Syphilis with Penicillin. N. Getzler.—p. 169.
Aspiration of Uterus as Competitive Method to Smear Curettage. O. Glück.—p. 173.
*Multiple Brain Tumors; Casuistic Contribution. H. Kraus.—p. 174.

Multiple Brain Tumors.—Kraus reports multiple brain tumors in a man aged 29 with bilateral neurinoma of the acoustic nerve (case 1), in a woman aged 67 with a left-sided neurinoma of the acoustic nerve and meningioma (case 2), in a man aged 26 with Recklinghausen's disease (case 3), in a man aged 25 with Recklinghausen's disease and meningioma (case 4), in a woman aged 44 with multiple meningiomas (case 5) and in a woman aged 19 with multiple gliomas (case 6). The first 2 patients died within ten days after admission to the hospital, before any surgical intervention had been carried out. The diagnosis of a bilateral tumor of the acoustic nerve is more difficult than that of a unilateral tumor, because comparison between left and right ventriculography does not reveal any differences. Observation in the first case revealed that dorsal displacement of the aqueduct may be shown on ventriculographic examination in bilateral medial neurinoma of the acoustic nerve. Surgical treatment was attempted in case 3, but operation was discontinued because of profuse hemorrhage. Diagnosis of Recklinghausen's disease may be easy if neurinomas are demonstrated simultaneously in the peripheral nerves as they were in case 3 and 4. Both patients were operated on, and both died soon after. The patient in case 4 did not present choked disk or signs of increased pressure, in spite of the considerable size of the neurinomas. The fifth patient was operated on successfully; four large and twelve small meningiomas with a total weight of 200 Gm. were removed from the brain, and one meningioma was removed from the spinal cord several weeks later. Satisfactory results may be obtained from extensive and radical intervention in multiple meningiomas, but recurrences must be anticipated. The sixth patient died after ventriculostomy had been performed. Necropsy revealed the rare simultaneous occurrence of glioma of the brain and of the spinal cord.

Book Notices

Synopsis of Psychosomatic Diagnosis and Treatment. By Flanders Dunbar, M.D. With the Assistance of Jacob Arlow, M.D., and others, and Members of the Staff of the Departments of Medicine and Psychiatry, Columbia-Presbyterian Medical Center, New York City. Fabrikoid. Price, $6.50. Pp. 501, with illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

In this book many of the leaders in the field of psychosomatic medicine combine to teach their subject on the basis of cases studied in various clinics. The book should be of special interest to the general practitioner who is interested in the technic of this approach to medical problems.

Textbook of Anatomy and Physiology. By Diana Clifford Kimber and Carolyn E. Gray, A.M., R.N. Revised by Caroline E. Stackpole, A.M. and Lutia C. Leavell, R.N., Assistant Professor in Nursing Education, Teachers College, Columbia University, New York. Twelfth edition. Cloth. Price, $4. Pp. 773, with 360 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1948.

This is a new revision of the well known text by Kimber and Gray. Since the last edition, the total number of figures has been increased by seven and the pages by four. There has been some revision of text, legends and cross references. A great deal of material is presented in concise form. In general, the selection of material is good. One omission is unusual: The small muscles of the hand are barely mentioned, whereas the small muscles of the foot are given in detail in the muscle summary and are shown in two illustrations.

Introduction to Physical Biochemistry. By J. M. Johlin, Ph.D., D.Sc., Associate Professor of Biochemistry in the Vanderbilt University School of Medicine, Nashville, Tenn. Second edition. Cloth. Price, $3.75. Pp. 246, with illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33d St., New York 16, 1949.

The author has presented an elementary discussion of some principles of physical chemistry and of their application to biochemistry (principally to the chemistry of blood). The amount of detail presented in the discussions of concepts and theories is meager in some cases, copious in others. There is much valuable information for the biochemistry student. It is unfortunate that the presentation is not as clear as might be desired.

Der Rücken des Menschen, die Erkennung und Behandlung Seiner Erkrankungen: Eine Anleitung für Studierende der Medizin und parktische Aerzte. Von Prof. Dr. med. O. Veraguth, gewesenem Direktor des Universitäts-Institutes für physikalische Therapie in Zürich, und Dr. med. C. Braendli-Wyss, Arzt in Burgdorf (Bern). Unter Mitarbeit von Dr. med. E. Frauchiger, Professor für vergleichende Neurologie an der Universität Bern. Second edition. Cloth. Price, 24 Swiss francs. Pp. 225, with 94 illustrations. Hans Huber, Marktgasse 9, Bern 16, 1948.

This book will be of limited interest to the readers of THE JOURNAL. The author discusses anatomic, neurologic, topographic and postural disturbances of the human back. There are some instructive illustrations in the book.

Treatment in General Practice. By Harry Beckman, M.D., Professor of Pharmacology, Marquette University School of Medicine, Milwaukee. Sixth edition. Cloth. Price, $11.50. Pp. 1129, with illustrations. W. B. Saunders Co., 218 W. Washington Square, Philadelphia 5, 1948.

The intensified rapid progress of medicine makes necessary far more frequent revisions of textbooks than were formerly necessary. In the present edition of this well established work, some sections have been rewritten entirely because of new information and the entire book has been brought up to date. The succinct and didactic method of presentation makes this book outstanding as a guide to general practitioners.

Inmovilización: Vendajes—tracción continua—enyesados. Por el Dr. José Pedro Reggi, profesor adjunto de la Facultad de ciencias médicas de Buenos Aires. Cloth. Pp. 326, with 382 illustrations. Lopez & Etchegoyen, S.R.L., Junin 863, Buenos Aires, 1948.

This book is of limited interest to the readers of THE JOURNAL. The author has drawn freely from the writings of authors from many countries. He favors the work of Watson-Jones of England and Bohler of Austria. The material, which is elementary, includes information on bandages, slings, adhesive, casts, apparatus, splints, wiring of teeth, traction, suspension, skeletal traction, tongs and Stader apparatus.

Outwitting Your Years. By Clarence William Lieb, M.A., M.D. Cloth. Price, $2.75. Pp. 278. Prentice-Hall, Inc., 70 Fifth Ave., New York 11, 1949.

Leisure is one source of temptation. When a physician retires, not the least of his temptations is to write another book on aging wherein he may once more display his wit and wisdom, give counsel, reiterate certain pet anecdotes concerning some more or less famous patients and indulge in a little wishful thinking in order to reassure himself that his own senescence is not as bad as he fears it is. Such indulgence can make pleasant reading. Dr. Clarence Lieb's style is charming, freely flowing and intimately conversational. His discussion of the major "facts of life" as they apply to senescence and senescents is sound, though the organization of his material is rather confused. For example, arthritis, neuritis, prostatitis and the need for ample time for convalescence are all brought together.

The book should prove particularly helpful to those who fear old age and, lacking the courage or imagination to face it realistically, find solace in such sedative philosophies as those of Coué, Christian Science or the more conventional dependency on religion. The truly mature—emotionally as well as somatically grown up—will find little therein of value to themselves.

The Spleen and Hypersplenism. By William Dameshek, M.D., & Solomon Estren, M.D. A Reprint of an Exhibit Presented at the 100th Anniversary Convention of The American Medical Association, Atlantic City, June 1947. Loose Leaf. Paper, $4.75. No pagination, with illustrations. Grune & Stratton, 381 Fourth Ave., New York 16, 1947.

Here in beautiful reproduction is the exhibit on this subject from the Hundredth Anniversary Convention of the American Medical Association in June 1947. The value of the book for teachers who are concerned with conditions affecting the blood and the spleen is exceedingly great. The work might well offer a suggestion to many other exhibitors, who could thus extend the excellent work they do by their exhibits in medical conventions.

West London Hospital Department of Rheumatic Diseases, Annual Report 1948. Paper. Pp. 40, with 13 illustrations. West London Hospital, London, [n.d.].

The rheumatism department of the West London Hospital was first opened in 1938 with the collaboration of the Empire Rheumatism Council. Since that time its work as a referral center has continuously increased except for the war. It is noteworthy that under miscellaneous "rheumatic" conditions referred to the department were included cases of multiple myeloma, osteomyelitis, herpes zoster, multiple sclerosis, acromegaly, myxedema, malignant diseases and scleroderma. As pointed out in this report, these figures emphasize the fact that a rheumatism department should be part of a general hospital and that workers in this field should have a solid training in general medicine.

Several interesting articles are included in this booklet which may not receive the attention they deserve because of its restricted circulation. One article, which was Dr. W. S. C. Copeman's Hunterian Oration, deals with the rheumatic diseases in the eighteenth century. Other papers are on psychogenic rheumatism by Dr. Philip Hench; on the action of salicylates by Fred. Wrigley, and on the differential diagnosis of prolapse of the "intervertebral disk" by Dr. R. M. Mason.

A Surgeon's Guide to Local Anæsthesia: A Manual of Shockless Surgery. By C. E. Corlette, M.D., Ch.M., F.R.A.C.S., Consulting Surgeon, Sydney Hospital, Sydney, Australia. Cloth. Price, $8.50. Pp. 355, with 200 illustrations. Williams & Wilkins Company, Mt. Royal & Guilford Aves., Baltimore 2, 1948.

This book is written by a surgeon who has learned the valuable lesson of doing surgical operations with local anesthesia. This has permitted him to develop a technic that is important in avoiding shock. He has made full use of epinephrine, both to anchor the anesthetic and to reduce hemorrhage. Preliminary medication he has relied on, as should be done, in cases in which major operations of considerable duration must be performed with local anesthesia.

The book is written entirely from the point of view of the surgeon who has mastered a technic of local anesthesia so thoroughly that he can perform nearly all his operations without resorting to general anesthesia or, if general anesthesia

must be employed, little of the anesthetic agent need be used. The author obviously has found infiltration anesthesia to be the most reliable method of local anesthesia in the operations that he does.

Modern Trends in Public Health. Edited by Arthur Massey, C.B.E., M.D., D.P.H. Cloth. Price, $12.50. Pp. 581, with 42 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33rd St., New York 16, 1949.

In some respects, this volume can be considered a send-off for what is referred to in the foreword as the "national insurance scheme" put into effect in England in 1948. That it appears during a period of transition is emphasized in his foreword by Massey, who also points out that many of the subjects pertain to topics of current interest. Specific chapters that may be mentioned in that connection are those on "The Idea of a Family Health Club," "Social Medicine as an Academic Discipline," "Housing and the Home—The New Outlook," and "Health Centers in Their Relation to Social Medicine and Public Health."

An attempt is not made to survey the entire field of public health, but nevertheless a rather wide range of subjects is covered by the various authorities who have contributed to the twenty-three chapter symposium. Historical and analytic in their treatment, the writers have made important summary contributions that together provide an interesting and enlighening panoramic picture of where Britain stands as regards public health problems and in what direction and how far the nation may be expected to progress in the near future. Among the authors are consulting physicians, general practitioners, public and industrial health officers, laboratory specialists and university teachers. Indicative of the growing interest in occupational health is the fact that the subject is approached from two points of view, those of the teacher and of the physician actively engaged in industrial health consultative service.

Of special interest in providing data on progress and possible predictions of future advances are the chapters on atmospheric pollution, nutrition, school health service, mental health, chronic rheumatism, tuberculosis, health education and child health. Although direct comparison with American methods and standards is not always possible, readers in this country will find not only that the excellent discussions are of real interest but also that in numerous instances there are parallel problems for solution.

Extensive bibliographies and references are included with most chapters. This will be a most interesting book to reread ten years from now.

Cottonseed and Cottonseed Products: Their Chemistry and Chemical Technology. Edited by Alton E. Bailey. Fats and Oils: A Series of Monographs on the Chemistry and Technology of Fats, Oils, and Related Substances. Editorial Board: A. E. Bailey, T. P. Hilditch, H. E. Longenecker and K. S. Markley. Cloth. Price, $17.50. Pp. 936, with 208 illustrations. Interscience Publishers, Inc., 215 Fourth Ave., New York 3, 1948.

This monograph, dealing with the chemistry and technology of cottonseed, is written by some twenty-five different authors, each treating a different phase of the cottonseed industry.

The book is divided into five general topics, each of which has several chapters. The first section deals with the history of the cottonseed industry and its present status in the various cotton-producing countries of the world. The second and largest section treats in detail the composition and characteristics of cottonseed. This includes sections on the structure of the seed, conditions affecting cottonseed composition, the biologic processes of cottonseed and the various chemical constituents which have been found in cottonseed. The grading and evaluation of cottonseed and its primary products—oil, cake, meal and linters—are discussed in the third section, while the fourth general topic is that of cottonseed processing; that is, the methods used to obtain the primary products. The final section deals with the utilization of the various primary products obtained from the seed. The refining processes are discussed and the nutritional aspects of both oil and meal are treated.

The volume is comprehensive in its scope, treating almost all possible aspects of cottonseed and its products. Its value is enhanced by its numerous footnote references and by fairly complete author and subject indexes.

Lehrbuch der Embryologie. Von Walter Brandt, M.D., Ph.D. Cloth. Price, 56 Swiss francs. Pp. 648, with 472 illustrations. S. Karger, Holbeinstrasse 22, Basel, 1949.

For many years premedical students studied embryology as a part of their general education in zoology and as a necessary, often tedious approach to an understanding of human anatomy. In the different medical schools varying degrees of attention are paid to embryology, although the courses in obstetrics usually stress the study of early human embryos with particular reference to implantation and placentation. As descriptive embryogenesis, even of the mammals, covers such a vast field, it is natural that many interesting topics receive but scant attention. It is interesting, and heartening to teachers of embryology, that with the advent of surgery of developmental defects of the heart, the embryogenesis of the organ has become a focus of interest to many medical students and especially to young physicians. This subject, formerly considered dry and uninteresting, and usually covered in a cursory manner, is now an important medical topic. The present extensive volume, in German, with a combined morphologic and dynamic approach to embryology, was aimed at supplying the needs of the medical student. There are numerous summaries of the accomplishments of experimental and comparative embryology, in addition to a detailed presentation of the morphogenesis of the human embryo. Among the most interesting parts of the book are the diagrams showing relative growth rates in the different parts of the body. The observations on very early human embryos and the thorough study of primate development in this country have greatly advanced the gaps in our knowledge of the early stages of human development, and these topics are well covered in the present text. The book can be recommended to anyone seeking a presentation of human embryogenesis as an active process. As a text for students in this country, it does not appear to be superior in any way to several of the English and American books now available.

Kurzgfasstes Lehrbuch der Erkrankungen des Ohres, der Nase und des Halses. Von Dr. med. Alfred Güttich. Boards. Price, 16 marks. Pp. 257, with 126 illustrations. Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1948.

This work is an example of the sort of short text for practitioners in which the Germans excelled in the period before the last war. It is authoritative, concise and well illustrated and contains enough of anatomy, pathology and theoretical considerations to make it understandable. Obviously, conditions in Germany during the war years and since have not been favorable for scholarship and its enterprises. The impact of the sulfonamide drugs, penicillin and the numerous other antibiotics which have changed the aspect of whole categories of disease does not seem apparent in this work.

The mention of the sulfonamide drugs and penicillin, in fact, is hardly more than casual, almost deprecatory and with allusion to the dangers of the so-called masking effect. There seems to be hardly any understanding that acute mastoiditis and its complications, for example, have practically disappeared. This applies, in part, to many of the other acute inflammations in the area of the ear, nose and throat.

This is not to say that such texts as these are without value. For the basic information as to the manner in which disease enrolled itself prior to the antibiotic days is here. If one may be permitted a melancholy reflection, it is sad to think how far behind that country is today, whose investigators and teachers did so much to establish this special field of medicine. It is sad to think, too, that the socioeconomic upheavals which followed the war, as they can faintly be judged by this work, have prevented large numbers of sick from obtaining the safety and relief which are seen here in America every day since the amazing advances of the last few years in chemotherapeutics.

The Chemistry and Technology of Enzymes. By Henry Tauber, Ph.D. Cloth. Price, $7.50. Pp. 550, with 56 illustrations. John Wiley & Sons, Inc., 440 4th Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C. 2, 1949.

The current volume replaces the author's "Enzyme Chemistry" and "Enzyme Technology" (Wiley, 1943). Part I is a summary of enzyme chemistry. The author has covered types of enzymes and specific enzymes extensively. The treatment is

necessarily not exhaustive, but many references to an extensive bibliography offer ready access to more detailed works.

Part II deals with the technology of enzymes. Processes discussed include the production of yeasts and enzymes and the production and properties of antibiotics, as well as the role of enzymes in alcohol production, baking, brewing, dairy and other food products, medicine, paper, textile and many other industrial applications. Chapters on microbiologic methods for the estimation of vitamins and amino acids and on vitamin-destroying enzymes are included. The author has presented an excellent and thorough treatment of this little publicized field of enzyme technology.

Food Poisoning. By G. M. Dack, Ph.D., M.D., Professor of Bacteriology and Director, Food Research Institute, The University of Chicago. Second edition. Cloth. Price, $3.75. Pp. 184. University of Chicago Press, 58th St. & Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W. 1; W. J. Gage & Co., Ltd., Toronto 2B, Canada, 1949.

The University of Chicago Press offered Dack's book six years ago as the first compilation of a class of etiologically scrambled diseases in which intestinal absorption of poisons, usually bacterial, appears to be the common factor. The book is now revised at many points, none radically, all sufficiently so that readers can be assured that they have recent points of view.

The author's refusal to become overenthusiastic on any phase or participate in the dogma of such bacteriologic Frankensteins as the Salmonella group does him credit. It is still uncertain whether only live Salmonella can cause food poisoning; in fact, laboratory experiments tend to prove otherwise. The weight of expressed epidemiologic opinion, however, appears against an enteric toxin acting without infection. The acute toxic symptoms and frequent short period of incubation remain more than suggestive of intoxication, and, with Salmonella common in eggs, poultry, slaughterhouses and rodents, the infrequency of infection is not explained.

The Staphylococcus problem is not solved. Bacteriophage and other means of typing are all entertaining, but we still cannot recognize enterotoxigenic staphylococci by simple means. The place of the Streptococcus viridans group in food poisoning is not yet clear. The purification of the toxin of botulism has not been turned to practical account, at least not under the oath of Hippocrates.

The charm of the book is in its balance. Clinical diagnosis, laboratory diagnosis, prevention and control, and discussions of etiology and pathogenesis are woven together in an effective and useful pattern.

This book is a concise, comprehensive, current evaluation of the subject of food poisoning and food infection. An excellent and convenient reference for the practising physician, health officer, epidemiologist, sanitarian, food laboratory technician and commercial food products manufacturer.

Die Pathologie des Stammhirns und ihre vegetativen klinischen Bilder, als Erkenntnis und Grundlage der Unfallbegutachtung innerer Krankheiten. Von Wolfgang H. Veil und Alexander Sturm. Second edition. Boards. Pp. 444, with 58 illustrations. Gustav Fischer, Jena 15, 1946.

This is an excellent volume on the nervous connections and pathology of the endocrine glands. The title is slightly misleading; one would expect to find the same sort of material as in English in the books of Weil, Wertham, Hassin or Freeman. Instead the material is largely clinical, and there is almost no discussion of micropathology. Approximately 120 case histories are given. Much of the material is irrelevant.

Although this book was published in 1946 the authors were apparently not in touch with developments in psychosomatic medicine in this country.

Mikro-Methoden: Zur Kennzeichnung organischer Stoffe und Stoffgemische. Von Dr. phil. et med. Ludwig Kofler und Dr. phil. et med. Adelheid Kofler. Boards. Pp. 337, with 151 illustrations. Universitätsverlag Wagner, Innrain 27, Postfach 219, Innsbruck, 1948.

The authors have compiled information on the methods and applications of fusion analysis using a micro melting point apparatus. The apparatus is an electrically heated metal block with a temperature-indicating device and provisions for illuminating and viewing a few crystals of the substance under examination. These are mounted and examined through the microscope during the heating and cooling cycles.

The technics are simple, and the methods are rapid and surprisingly accurate. Methods are described for the determination of melting points, molecular weights, sublimation temperature, refractive index of the melt and qualitative analysis of pure compounds and mixtures. Qualitative analysis is effected by determining the melting point of the pure compound, the eutectic point of mixtures of two known compounds with the unknown, and the refractive index of the melt. Other observations often include such factors as crystal shape, sublimation and appearance of the sample after melting and cooling to recrystallization.

Tables of data for qualitative analysis are given for about 1,000 compounds. This is far from a complete list, but it does include most of the common solid organic compounds. Sufficient constants are included to identify each unknown rather definitely.

Emergency Surgery. Part I; Part II. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.I.C.S., Surgeon and Surgeon-in-Charge of the Genito-Urinary Department, Royal Northern Hospital, London. Sixth edition. Cloth. Price, $25., per set of five parts. Pp. 180, with 289 illustrations; 181-388, with 290-612 illustrations. Williams & Wilkins Co., Mount Royal & Guilford Aves., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1948.

This book has been completely revised and is now appearing in five parts. The introduction is especially worth reading, for the philosophy of the surgeon who is ready to serve in emergencies.

Part I deals chiefly with transfusion and clysis. Possibly the most valuable discussion concerns drainage. When a master surgeon so definitely expounds his views in such a controversial field, he deserves attention. Every surgical resident should read the chapter on drainage.

Part II deals with perforation of a peptic ulcer and its treatment. Cholecystitis and cholelithiasis are well covered. The author does not favor emergency cholecystectomy in acute cholecystitis. In this country such an operation performed early in selected cases has yielded excellent results. Intestinal obstruction receives fair attention. The etiology and surgical procedures are thoroughly described. However, while the author does mention treatment with intestinal intubation and electrolyte replacement, he does not emphasize these vitally necessary technics.

Modern Foot Therapy. By Reuben H. Gross, M.Cp., Pod.D., Dean, and Chairman, Department of Podiatry, The First Institute of Podiatry, Long Island University, Brooklyn, N. Y. In collaboration with Henri L. DuVries, M.D., Professor of Surgery, The Illinois College of Chiropody and Foot Surgery, Chicago, and others. With chapters by Martin Blass, Pod.D., and others. Edited by Maurice J. Lewi, M.D., President, and Director of Instruction, The First Institute of Podiatry, Long Island University, Brooklyn, N. Y. Cloth. Price, $9.50. Pp. 710, with illustrations. Foot Therapy Publishing Co., 55 E. 124th St., New York 35, 1948.

This book, written in monographic style with the help of numerous collaborators, covers too large a field for a book on podiatry. Much material is not within the purview of the podiatrist. This book is also entirely too complicated and too high sounding; for example, the words "dysbasia pododynia." The erroneous statement is made that weak foot is never cured. Many of the illustrations are poor. The figure of spina bifida is extraneous in a book of this type.

Cardiac Catheterization in Congenital Heart Disease: A Clinical and Physiological Study in Infants and Children. By André Cournand, M.D., Associate Professor, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, Janet S. Baldwin, M.D., Assistant Professor, Department of Pediatrics, New York University College of Medicine, and Aaron Himmelstein, M.D., Instructor, Department of Surgery, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $4. Pp. 108, with illustrations. The Commonwealth Fund, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London, E.C. 4, 1949.

This monograph will serve as an excellent primer for those who wish to familiarize themselves with cardiac catheterization in infants and children. The first part of the book outlines the technic involved and the information to be obtained from this method of study. The second part includes seventeen illustrative cases in which clinical studies have been combined with the results from catheterization in arriving at a diagnosis of congenital cardiac malformations.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VACCINATION AGAINST SPOTTED FEVER

To the Editor:—A family who has been under my care is planning to spend a vacation in Idaho in an area where Rocky Mountain spotted fever is prevalent. They have been informed that it would be wise for them to have a vaccination or serum injection prior to the intended trip. I would like information concerning prophylactic serum, how to give it and what results can be expected. Bernard H. Ailts, M.D., Sweetwater, Texas.

ANSWER.—The Rocky Mountain spotted fever season corresponds to the prevalence of the tick, Dermacentor andersoni in the West and Dermacentor variabilis in the East. In the Rocky Mountain region this season is roughly from March until the middle of June, and in the East from May until the middle of August. It is advisable to complete immunizations about a week or ten days before expected exposure to ticks. The vaccine is available commercially from several of the biologic laboratories and is prepared from the membranes of infected chick embryos. It is usually given as two injections, a week apart, and a booster dose seasonally thereafter. Since the vaccine contains protein from the embryo, a careful history should be taken to rule out possible sensitivity to chicken proteins. The U. S. Public Health Service laboratory at Hamilton, Mont., prepares a limited amount of vaccine each year from the tissues of infected ticks, which can be secured for those patients unable to take the chick embryo material because of sensitivity.

Now that there are two antibiotics available, chloromycetin® and aureomycin, for the treatment of Rocky Mountain spotted fever, the necessity for vaccination against the disease has decreased somewhat.

TREATMENT OF HEPATOMEGALY

To the Editor:—What measures may be of value in treatment of hepatomegaly associated with auricular fibrillation and congestive disease of long standing, aside from adequate digitalis and mercurial diuretics?

Charles Hertzman, M.D., New York.

ANSWER.—Hepatomegaly associated with congestive disease may be due to one of three pathologic processes: simple chronic passive congestion, "nutmeg liver" (cyanotic atrophy) or hepatic fibrosis (cardiac cirrhosis). The first two conditions will as a rule respond to the measures usually employed in the treatment of the underlying cardiac lesion; these include mercurial diuretics, digitalization and, perhaps most important, a diet low in sodium. An exception has to be made in the occasional case of adherent pericardium, in which the situation may be complicated by the so-called pericarditic pseudocirrhosis of Pick with its characteristic hyperplastic perihepatitis.

The existence of cardiac cirrhosis has been disputed, but many authorities now are of the opinion that from 1 to 7 per cent of the large livers seen in patients with repeated bouts of congestive disease will show a considerable amount of hepatic fibrosis and thus resemble classic Laennec cirrhosis. The condition is difficult, if not impossible, to recognize during life; a persistently low content of albumin in the serum, macrocytic anemia, hypoprothrombinemia and positive results of flocculation tests with thymol reagents or zinc sulfate are suggestive but not necessarily diagnostic. In case of doubt a diet high in protein, vitamin supplements and parenteral liver extract may be useful in treatment.

ANTISEPTICS AND VIRUSES

To the Editor:—What effect do the organic mercurial antiseptics have on filtrable viruses, in the tincture and in aqueous sol? M.D., Ohio.

ANSWER.—Few viruses have been tested in a pure state against chemical and other agents. They are resistant to the action of phenol and related disinfectants; coal tar disinfectants are said to be somewhat more effective for their inactivation. Cutting and his co-workers (*J. Bact.* **57**: 379, 1947) reported many substances, including alcohols, dyes, metallic compounds and organic acids, ineffective when tested in vivo against virus infection in mice or embryonated eggs. Because of the variable response of the viruses to chemical agents, heat or ultraviolet irradiation are the preferred methods for their destruction. The viruses are also readily destroyed by alkalies.

AXILLARY SWEATING

To the Editor:—What is the most satisfactory method of managing perspiration under the armpits? M.D., Indiana.

ANSWER.—Drugs taken internally are not practical for reducing axillary sweating. Atropine is more active against eccrine sweating; that is, sweating other than from specialized glands in the axillas, at the pubis and a few elsewhere. In sufficient dosage to be effective this drug may have unpleasant side reactions. Therefore local applications are the best means for managing perspiration under the arms.

Topical applications attempt to accomplish one of two results—to overcome or mask the objectionable odor or to reduce the amount of sweat. Astringents are usually used for the latter purpose. They include such materials as tannic acid and the tannates in general, formaldehyde, zinc salicylate, aluminum chloride and aluminum phenolsulfonate. These may be irritating and formaldehyde is a common sensitizer to the skin. Aluminum salts may be destructive to clothes, but buffering them with urea helps to overcome this fault.

The deodorizing agents include hexamethylenetetramine, sodium perborate, zinc peroxide, oxyquinoline sulfate and others. They may be used in solutions, creams and powder mixtures. Essential oils and perfumes are used as masking materials. Hexamethylenetetramine may irritate and sensitize. Lamb has found sodium bicarbonate powder mixtures deodorant.

IRIDOCYCLITIS

To the Editor:—What are the latest opinions concerning the causation and treatment of iridocyclitis? Can it be allergic in origin? What are the possibilities of the uninvolved eye's becoming affected? When is it advisable to remove the affected eye?

Charles Hertzman, M.D., New York.

ANSWER.—Iridocyclitis may be divided into granulomatous and nongranulomatous types. The granulomatous type is characterized by an insidious onset, a torpid course, minimal inflammatory signs and resistance to treatment. The lesion is profoundly modified and influenced by factors of local hypersensitivity and general immunity. This type of inflammation may be due to tuberculosis, syphilis, brucellosis, sarcoidosis, leprosy, sympathetic ophthalmia or herpes zoster ophthalmicus. Nongranulomatous iritis occurs with dramatic rapidity, with inflammation and pain, but tends to clear up quickly without residue. Recurrences are frequent. This type of inflammation frequently follows systemic infections and may be due to organisms arising in a focus of infection or may occur in conjunction with rheumatoid arthritis or gonorrhea. Ocular sensitization to a strain of the streptococci, staphylococci or Neisseria gonorrhoeae is considered the cause.

Treatment is specific when possible, or directed toward desensitization of the ocular tissues if hypersensitivity is demonstrated. Injections of foreign protein, artificial fever, salicylates or antibiotics may be indicated. Pupillary dilation with atropine should be done after acute congestive glaucoma as the cause of the symptoms has been excluded.

Involvement of the opposite eye depends on the cause of the disease. It is usually not necessary to remove the affected eye except when it is blind and painful.

DRIVER'S LICENSE

To the Editor:—1. When is it safe to recommend the restoration of a driver's license to one who has suffered with a convulsive disorder? 2. What criteria should be used in formulating an opinion?

Diomede Guertin, M.D., Skillman, N. J.

ANSWER.—1. A convulsive disorder is a rather ambiguous term and provides too much latitude for accurate answering of the question. If it is assumed that the convulsive disorder is to be construed as one of the group of cryptogenic epilepsies, then the answer can be based on experiences gathered to date by workers in this field. It is generally felt that a patient who is under complete control for at least one year should be a safe driver. It is to be assumed that in maintaining his license he will remain under such medical control as to continue to keep seizure free.

2. Accurate historical data from the patient and members of his family, such other social information as can be obtained and electroencephalographic studies at yearly intervals. It must be born in mind, however, that patients clinically free of seizures may continue to show electroencephalographic disturbances, but as the electroencephalogram shows improvement or return to normal, it can be assumed that the outlook for control is highly favorable.

CONCENTRATION OF FREE SERUM CHOLESTEROL

To the Editor:—Clinically, various types of injury to the organism (severe acute infection, for example) are known to be accompanied by a decrease in the concentration of serum-free cholesterol and serum cholesterol esters. This may be reproduced in the laboratory with the aid of a number of nonspecific damaging agents. (Acute hemorrhage, however, is an exception and causes an increase in serum cholesterol.) Recent experimental work suggests that the fall in serum cholesterol during acute stress may be closely related to altered adrenocortical function in such circumstances. Recently, under conditions where it was not possible to study hormone excretions directly, we attempted to use indirect methods of judging adrenocortical status. One of the data to be interpreted was a decrease in serum cholesterol values under a particular type of stress. In reviewing the literature on this topic we were unable to find any definite statement on whether patients with Addison's disease or adrenalectomized animals, otherwise suitably maintained, do or do not show the usual fall in serum cholesterol concentration when exposed to infection or other types of stress with organismic damage. Can you supply information on this topic?

M.D., Illinois.

ANSWER.—The literature concerning blood cholesterol changes in adrenalectomized animals and patients suffering from Addison's disease contains many contradictory statements. Apparently, the response is largely dependent on the diet, the degree of adaptation to stress and other factors. In adrenalectomized animals, both abnormally low and abnormally high values have been reported, although in the rabbit, after adrenalectomy, the blood cholesterol almost invariably rises in a significant manner.

In Addison's disease, the cholesterol content of the blood is usually decreased, according to Marañón. He claims that the decrease in blood cholesterol runs parallel with the severity of the clinical symptoms. In later publications, Marañón and Collazo confirmed the frequent occurrence of hypocholesterolemia in numerous cases of Addison's disease, and they found, furthermore, that injections of cortin restore the blood cholesterol to normal. Medvei observed an increase of the blood cholesterol content in 4 cases of Addison's disease.

Data concerning the influence of cortical steroids and crude cortical extracts are likewise contradictory. It is interesting, however, that in rats sensitized to the toxic actions of desoxycorticosterone by unilateral nephrectomy and a high sodium chloride intake this steroid consistently produces an elevation of blood cholesterol.

PREVENTION OF DENTAL CARIES

To the Editor:—The January 9 issue of *Collier's* had an article on a new dental prophylaxis with zinc chloride–potassium ferrocyanate. Please give the latest opinion concerning fluoride prophylaxis and evaluate the new method mentioned.

James E. Wheeler, M.D., Newtown Square, Pa.

ANSWER.—With respect to the topical application of a fluoride solution as a prophylaxis against dental caries, present knowledge would suggest a reduction of about 40 per cent in the group treated. It is essential that the teeth be thoroughly cleaned with pumice (oral prophylaxis) before the first application of the 2 per cent sodium fluoride is made. A minimum of four treatments, which may be given a week apart, is essential.

The zinc chloride–potassium ferrocyanate technic, commonly referred to as the Gottlieb impregnation technic, which was recently reported in *Colliers,* was recently reviewed by the Council on Dental Therapeutics of the American Dental Association. In the January 1949 issue of the journal of that association (pp. 147-148) after reviewing the background and the changes that have occurred in the technic, they state: "As far as the Council can ascertain, the effectiveness of preparations that have been suggested for use in impregnation has not been established. The Council will be pleased to receive further evidence concerning the value of these preparations and will modify its appraisal if their merit is scientifically established."

ACIDIFYING AGENTS AND SODIUM-POOR DIETS

To the Editor:—Please comment on whether the oral administration of dilute hydrochloric acid or ammonium chloride acts synergically to a salt-poor and salt-free diet.

R. R. Gutstein, M.D., Kendallville, Ind.

ANSWER.—Dilute hydrochloric acid and ammonium chloride can aid treatment with low sodium diets, either at the outset by accelerating sodium depletion or during the course by maintaining it when dietary control is not sufficiently rigid. The initial effect is urinary acidification with increased secretion of hydrogen ion by tubule cells; secondarily, as the urine becomes strongly acid, sodium is lost into the urine with the excess chloride ion; the final mechanism is compensatory. It consists in increased secretion of ammonium ion by tubule cells. The secretion of ammonia increases to a maximum in three to four days, at the end of which the acidifying agents have little effect in causing sodium depletion. Consequently, for their most efficient use, acidifying agents should be prescribed discontinuously, as, for example, for three days in each week.

In the presence of renal disease, evidenced by failure of urinary concentrating power, administration of sodium-poor diets is in some degree hazardous, since the renal mechanisms for sodium retention are presumably defective. The hazard is greatly increased by use of acidifying agents. This is due to the concurrent failure of the mechanisms of secretion of hydrogen and ammonium ions.

There is some evidence that pregnancy is associated with decreased effectiveness of the mechanisms which protect against acidosis. Here again, the combination of low sodium diets and acidifying agents imposes the danger of acidosis and hyponatremia. With these provisions, the use of an acidifying agent such as ammonium chloride (this in doses of about 1 Gm. four times daily, three days in the week) is a logical adjuvant to treatment with sodium-poor diets.

RESERVOIR FUNCTION OF SPLEEN

To the Editor:—A boy aged 11 was injured in an automobile accident six months ago. His parents state that he was taken to a nearby hospital in an unconscious state but rapidly regained consciousness and complained of pain in the abdomen and left shoulder. Laparotomy was done and a ruptured spleen was removed. He was discharged from the hospital about ten days later apparently well, but the parents state that since the accident he is unable to indulge in strenuous athletics. He tires readily on overexertion but not on moderate exertion. The hemoglobin is normal, (11 Gm. per hundred cubic centimeters), and his differential, white blood cell and thrombocyte counts are within normal limits. The question now arises of partial permanent disability following splenectomy for trauma. As the spleen acts as a reservoir of red cells, contracting on demand, is it probable that the loss of this function could produce abnormal fatigue from strenuous exercise?

Thomas Bradley, M.D., Washington, D. C.

ANSWER.—It is generally accepted that severe muscular exertion is accompanied by a slight and transient rise in the red blood corpuscles. According to Barcroft, the spleen acts as a reservoir for red cells in animals and during exercise it contracts and discharges cells into the circulation. In man, there is evidence that the spleen does not have a reservoir function. Ebert and Stead (*Am. J. M. Sc.* **201**: 655, 1941) found that exercise caused an increase in the hemoglobin and volume of packed cells in both normal and splenectomized persons and that this was associated with a decrease in plasma volume. Nylin (*Am. J. Physiol.* **149**: 180, 1947), using red cells labeled with radiophosphorus, observed no change in the total circulating red corpuscles after heavy work. The abnormal fatigue experienced by the patient in the query is probably not related to a loss of a reservoir function of the spleen.

RHEUMATIC VALVULAR DISEASE

To the Editor:—A sturdy young man, age 34, came to my office complaining that his heart missed a beat occasionally. He said that he had acute rheumatic fever with definite heart disease at age 17. He lost a year of school on this account but made such a good recovery that he was accepted for all high school athletics, even playing on the football team. He has not had another attack of rheumatism since, has enjoyed perfect health and can do hard work. He is 6 feet 1¼ inches (186 cm.) tall and weighs 165 pounds (74.8 Kg.). He has a loud diastolic murmur, loudest below the apex, not transmitted to the axilla or the back. The left border of the heart is 1 cm. outside the nipple line. At the age of 17 he measured, on a physician's scales, 6 feet 3 inches (190.5 cm.). How do you account for a decrease in height of 1¼ inches in a young man of his age without spinal trouble? Is his record of rheumatism and mitral stenosis unusual?

A. T. Blackly, M.D., Portland, Ore.

ANSWER.—An explanation for the slight shrinkage in this young man's stature is not apparent. It may be added, however, that there may be normally a decrease in height up to 1 inch (2.5 cm.) in the average person at the end of the day as compared with measurements taken shortly after arising in the morning.

The record is not remarkable as regards the rheumatic history and subsequent valvular disease. It is well known that during acute rheumatic fever murmurs suggestive of valvular disease may subsequently disappear. It is also well known that years later the characteristic signs of mitral stenosis may appear without necessarily recognizable intervening rheumatic activity.

References:

Bland, E. F.; Jones, T. D., and White, P. D.: Disappearance of the Physical Signs of Rheumatic Heart Disease, J. A. M. A. **107**: 569 (Aug. 22) 1936.

Bland, E. F., and Jones, T. D.: The Delayed Appearance of Heart Disease After Rheumatic Fever, J. A. M. A. **113**: 1380 (Oct. 7) 1939.

INFECTIOUS MONONUCLEOSIS

To the Editor:—Is there any specific medication for infectious mononucleosis. The patient is a white girl, age 16, with nontender enlargement of cervical, submaxillary, submandibular and postauricular nodes. The throat is inflamed; the temperature is 100.6 F., and the spleen is not palpable. The diagnosis was confirmed by a white blood cell count of 17,800, with 69 per cent lymphocytes, of which 50 per cent were atypical.

M.D., New York.

ANSWER.—No specific therapy has yet been found for infectious mononucleosis. Aureomycin is said to have produced encouraging results in certain preliminary observations, but it is still too early for final conclusions. On the other hand, if the patient is treated in the same manner as a patient with viral hepatitis, both the severity and the duration of convalescence can be materially decreased. There is now ample evidence that hepatitis is almost always present in mononucleosis and is usually the most important pathologic lesion. The clinical picture and the course of the hepatitis are almost identical with those seen in viral hepatitis.

SOMNIFENE® IN OBSTETRICS

To the Editor:—What are the advantages and the disadvantages of somnifene® as an anesthetic in obstetrics? What is the best way of using it?

Denis Stein, M.D., Nouveau, Brunswick, Canada.

ANSWER.—Somnifene® (a mixture of the diethylamine salts of diethylbarbituric acid and allylisopropylbarbituric acid) has not been the subject of any paper in an American journal as far as is known. It has been mentioned in the French literature but not in recent years. In the 1936 Yearbook of Obstetrics and Gynecology, page 164, J. P. Greenhill says: "The study by H. Vignes and J. Chatain (*Presse méd.* **43**:1748, Nov. 9, 1935) deals with the effect of derivatives of barbituric acid, namely, evipan, somnifen, pernocton, etc., on labor pains. The authors found that the chief danger of these drugs was excitation of the patient, which occurred in about 25 per cent of all cases. It is possible to decrease this by the use of morphine and pantopon, but there may result an accumulation of the drugs dangerous for the baby. However, in a large proportion of cases the mothers are relieved of the pains of labor, especially during the second stage."

SENSITIVITY TO LIVER

To the Editor:—I have a patient who, many years ago, required blood transfusion regularly and then started taking liver. She took liver orally and later by injection. She has now an allergic reaction to liver. What can you suggest?

S. Bernard Ross, M.D., New York.

ANSWER.—It is assumed, of course, that the patient has pernicious anemia and therefore must have liver in some form. If the effective principle, vitamin B_{12}, can be obtained, this would probably be the best solution. Otherwise, it is sometimes possible, by trying a variety of different brands of liver extract, to find one to which the patient is not sensitive. Various methods of desensitization have been described, but they are only moderately effective.

CHRONIC BLEPHARITIS

To the Editor:—Can vioform® (iodochlorohydroxyquinoline), 1 per cent in an ointment vehicle, be used in treatment of chronic blepharitis?

Walter Weinberger, M.D., Altoona, Pa.

ANSWER.—Iodochlorohydroxyquinoline contains 41 per cent iodine. Because of its insolubility it does not cause gastrointestinal irritation or toxic effect when taken internally. The drug has been used as a nonirritating surgical powder, has been administered internally and in enemas as an amebacide, and applied locally for vaginitis due to Trichomonas. Three per cent in petrolatum or cream (water-washable base) has been employed for atopic dermatitis, eczema and psoriasis. There should not be an objection to use of 1 per cent vioform® in a petrolatum base for the treatment of chronic blepharitis.

PSYCHOSIS IN A MENTALLY DEFECTIVE PERSON

To the Editor:—What constitutes a psychosis in a mental defective patient? Can an idiot become psychotic?

W. W. Dreher, M.D., Whitfield, Miss.

ANSWER.—The criteria for psychosis in a mentally defective person are the same as those for other subjects. Any type of psychosis may develop, from confusional states to organic syndromes. The intellectual deficiency of mentally defective persons is not a psychosis. An idiot or any other mentally defective person may become psychotic.

RH INCOMPATIBILITY AND ABORTIONS

To the Editor:—A woman, age 43, married seventeen years, with Rh-negative Kahn-negative reactions, whose physical condition is excellent and genitalia normal, has had several pregnancies with spontaneous abortions occurring at two months, three months and four months. The husband is healthy, middle aged, with Kahn-negative and Rh-positive reactions. Is the Rh factor a contributing factor in her abortions and, if so, is there any method known to combat the incompatibility? This woman is desirous of bearing a child.

Walter R. West, M.D., Idaho Falls, Ida.

ANSWER.—Evidence is not available that Rh incompatibility is responsible for early abortions. The blood of the woman should be tested for Rh antibodies. Their presence would establish sensitization to the Rh factor, though not necessarily the responsibility of the Rh incompatibility for the abortions. A connection between the Rh incompatibility and the abortions could be established only by finding erythroblastosis in the fetuses by autopsy. However, even if Rh incompatibility were shown to be responsible for this woman's abortion, there is, at present, no known way of correcting the condition. Other possible causes of early abortions should be investigated.

TREATMENT OF VINCENT'S INFECTION OF THE MOUTH

To the Editor:—In Queries and Minor Notes, The Journal, April 23, 1949, page 1238, a question appears regarding recurrent oral Vincent's infection. The suggested treatment includes the use of silver nitrate solution following scaling. It also states that peroxide mouth washes have questionable value.

The use of a caustic (silver nitrate, chromic acid) as a general therapeutic agent in the treatment of Vincent's infection is frowned on. The destruction of tissue which results is nearly always permanently disfiguring.

Since spirilla and fusiform bacilli are found in many mouths not exhibiting signs of Vincent's infection, a smear should be used merely as a guide to diagnosis and is not pathognomonic.

The treatment which I have found uniformly successful follows:

An immediate scaling of the debris and affected areas, the extensiveness of scaling dictated by the patient's tolerance to pain. Scaling is accompanied with frequent spraying with hydrogen peroxide diluted 50 per cent with warm water. Penicillin troches are prescribed, or in acute conditions procaine penicillin, 300,000 units, may be injected intramuscularly.

Tobacco, alcohol, salt and spicy foods are prohibited at once. The patient is given a new toothbrush. Home care consists of frequent rinsing with hydrogen peroxide diluted 50 per cent with warm water.

After twenty-four hours, the patient commonly returns with all acute symptoms relieved. At this time intensive scaling is started. If there is found to be a malocclusion that can be corrected by grinding, this is done concomitantly with the scaling. Rough fillings, carious teeth, third molar flaps, poor fitting crowns and bridges all act as foci and incubation areas and are eliminated as soon as possible.

The office treatment, which consists of scaling and correction of occlusion, usually requires three to six visits. During this time the patient is instructed in home care, tooth brushing and oral hygiene, and advice is given regarding a balanced diet.

After a clinical cessation of symptoms, tobacco in moderation and normal dietary habits may be resumed.

Julius Schaffer, D.D.S., New York.

PROTEIN-BOUND IODINE

To the Editor:—Your answer to the question on page 814 of the March 19 Journal on protein-bound iodine is in error. Administered iodine, whether as Lugol's solution, gallbladder dye or inhaled iodine from spilled solutions, will raise the protein-bound iodine fraction. This should in no way interfere, however, with determination of the activity of the thyroid gland by use of blood iodine levels, since this technic properly done measures the falsely high bound iodine and then discards it through hydrolysis to give a figure that is the true index of the gland's activity. A case occurred at a New Haven hospital wherein the intern surreptitiously did an iodized oil study of the spinal canal to try to prove his diagnosis of tumor. The patient, who had myxedema, showed high total and protein-bound iodine levels for weeks. The significant protein-bound fraction remained in the myxedematous range.

L. S. Wolfe, M.D., New Milford, Conn.

To the Editor:—I think I can add to the information given by your consultant regarding the effect of gallbladder dyes on the protein-bound blood iodine.

In my paper "The Nature of the Blood Iodine and Its Determination" (*J. Lab. & Clin. Med.* **28**:329, 1942) the effect of a series of organically bound iodine compounds on the protein-bound blood iodine is reported. All these compounds increase the protein-bound blood iodine, and at present chemical methods are not available for separating this from the normally occurring protein-bound blood iodine. The usual methods that will separate inorganic iodine are not of avail. We have carried out studies showing that the protein-bound blood iodine is elevated for at least two months after a single dose of any of the commonly used gallbladder dyes. This is probably due to the recirculation of the dye following its excretion in the bile and reabsorption from the intestinal tract. For the information of your correspondent, I should say that significant determinations of the level of protein-bound blood iodine cannot be made by present methods for at least several months after the administration of a gallbladder dye.

Solomon Silver, M.D., New York.